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E. M. L.

THE BOSTON

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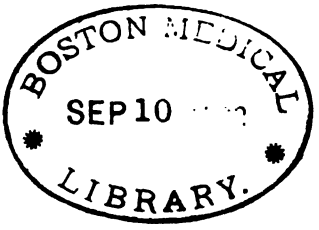

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1890	TIMOTHY HOLMES
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1894	JONATHAN HUTCHINSON
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HONORARY FELLOWS

(Limited to Twelve.)

Elected

1887 FOSTER, SIR MICHAEL, K.C.B., M.D., LL.D., F.R.S., M.P., Professor of Physiology in the University of Cambridge, Nine Wells, Great Shelford, Cambridge.

1868 HOOKER, SIR JOSEPH DALTON, M.D., C.B., G.C.S.I., D.C.L., LL.D., F.R.S., Corresponding Member of the Academy of Sciences of France; The Camp, Sunningdale.

1896 KELVIN, The Right Hon. LORD, G.C.V.O., F.R.S., Pres. R.S.E., D.C.L., LL.D., &c., Glasgow.

1878 AVEBURY, The Right Hon. LORD, D.C.L., LL.D., F.R.S., High Elms, Farnborough, Kent, R.S.O.

1873 STOKES, SIR GEORGE GABRIEL, Bart., M.A., D.C.L., LL.D., Sc.D., F.R.S., Lucasian Professor of Mathematics in the University of Cambridge; Lensfield Cottage, Cambridge.

1887 TURNER, SIR WILLIAM, M.B., D.C.L., LL.D., F.R.S., Professor of Anatomy in the University of Edinburgh; 6, Eton Terrace, Edinburgh.

FOREIGN HONORARY FELLOWS

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Elected

1878 Baccelli, Guido, M.D., Rome.

1896 von Bergmann, Ernst, Berlin.

1887 Billings, John S., M.D., D.C.L.Oxon., New York.

1896 Czerny, Vincent, M.D., Heidelberg.

1896 Erb, Wilhelm, M.D., Professor of Clinical Medicine, Heidelberg.

1887 von Esmarch, His Excellency Friedrich, M.D., Kiel.

1896 Fournier, Alfred, M.D., Paris.

1896 Gerhardt, Carl, M.D., Berlin.

1896 Koch, Robert, M.D., Berlin.

1896 Kocher, Theodore, M.D., Berne.

1868 Kölliker, Albert, Würzburg.

1896 Laveran, A., M.D., Paris.

1896 Marie, Pierre, M.D., Paris.

1896 Mirza-Ali, M.D., Teheran.

1896 Mitchell, Samuel Weir, M.D., Philadelphia.

1856 Virchow, Rudolf, M.D., LL.D., Berlin.

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OF THE

ROYAL MEDICAL AND CHIRURGICAL SOCIETY

OF LONDON

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P.—President.
V.P.—Vice-President.
T.—Treasurer.
L.—Hon. Librarian.
S.—Hon. Secretary.
C.—Member of Council.
Sci. Com.—Member of a Scientific Committee.
Ho. Com.—Member of House Committee.
Lib. Com.—Member of Library Committee.
Bldg. Com.—Member of Building Committee.
Dis. Com.—Member of Discussions Committee.

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Elected

1898 AARONS, S. JERVOIS, M.D., 14, Stratford place, Oxford street.

1877 **Abercrombie**, JOHN, M.D., Physician to, and Lecturer on Forensic Medicine at, Charing Cross Hospital; 23, Upper Wimpole street, Cavendish square. C. 1896-8. *Referee*, 1898—. *Trans.* 2.

Elected

1885 ABRAHAM, PHINEAS S., M.A., M.D., Dermatologist to the West London Hospital, Assistant Surgeon to Hospital for Diseases of the Skin, Blackfriars; 2, Henrietta street, Cavendish square.

1885 ACLAND, THEODORE DYKE, M.D., Physician to St. Thomas's Hospital, and Physician to the Hospital for Consumption and Diseases of the Chest, Brompton; 19, Bryanston square.

1897 ADDISON, CHRISTOPHER, M.D., Charing Cross Hospital Medical School, Chandos street.

1879 ALLCHIN, WILLIAM HENRY, M.D., F.R.S. Ed., Senior Physician to the Westminster Hospital; 5, Chandos street, Cavendish square. C. 1898-9. *Referee*, 1897.

1890 ALLINGHAM, HERBERT WILLIAM, Surgeon to His Majesty's Household, Surgeon to the Great Northern Hospital; Assistant Surgeon to St. George's Hospital; 25, Grosvenor street, Grosvenor square.

1888 ANDERSON, JOHN, M.D., C.I.E., Physician to the Seamen's Hospital, Greenwich; Lecturer on Tropical Medicine at St. Mary's Hospital Medical School; 9, Harley street, Cavendish square.

1891 ANDREWES, FREDERICK WILLIAM, M.D., Highwood, Hampstead Lane, Highgate.

1893 BAILEY, ROBERT COZENS, M.S., 21, Welbeck street. Cavendish square.

1891 BAKER, CHARLES ERNEST, M.B., 5, Gledhow gardens, South Kensington.

1899 BAKER, OSWALD, 57, Welbeck street, Cavendish square.

1900 BALDWIN, ASLETT, 6, Manchester square.

1887 BALL, JAMES BARRY, M.D., Physician to the West London Hospital; 12, Upper Wimpole street, Cavendish square.

1885 BALLANCE, CHARLES ALFRED, M.S., Assistant Surgeon to St. Thomas's Hospital and to the Hospital for Sick Children, Great Ormond street; Surgeon to the National Hospital for the Paralysed and Epileptic, Queen square; 106, Harley street, Cavendish square. *Trans.* 5.

Elected

1879 BARKER, ARTHUR EDWARD JAMES, Professor of the Principles and Practice of Surgery and Professor of Clinical Surgery at University College, and Surgeon to University College Hospital, London; 87, Harley street, Cavendish square. C. 1895-7. *Referee*, 1897—. *Trans.* 7.

1876 **Barlow**, SIR THOMAS, Bart., K.C.V.O., M.D., B.S., *Hon. Secretary, Trustee for Debenture-holders;* Physician to His Majesty's Household; Physician to University College Hospital; 10, Wimpole street, Cavendish square. C. 1892. S. 1899—. *Referee*, 1896-9. *Trans.* 2.

1893 BARRETT, HOWARD, 49, Gordon square.

1880 BARROW, A. BOYCE, Surgeon to King's College Hospital; 8, Upper Wimpole street, Cavendish square.

1896 BARTON, JAMES KINGSTON, 2, Courtfield road, Gloucester road, South Kensington.

1859 BARWELL, RICHARD, Consulting Surgeon to the Charing Cross Hospital; 55, Wimpole street. C. 1876-77. V.P. 1883-4. *Referee*, 1868-75, 1879-82. *Trans.* 12. *Pro.* 1.

1868 **Bastian**, HENRY CHARLTON, M.A., M.D., F.R.S., Emeritus Professor of the Principles and Practice of Medicine and of Clinical Medicine in University College, London; Consulting Physician to University College Hospital and Physician to the National Hospital for the Paralysed and Epileptic; 8A, Manchester square. C. 1885. *Referee*, 1886-96. *Trans.* 3.

1890 BATEMAN, WILLIAM A. F., Bridge House, Richmond, Surrey.

1891 BATTEN, FREDERICK E., M.D., B.C., 38, Harley street.

1875 BEACH, FLETCHER, M.B., Physician to the West End Hospital for Nervous Diseases, Winchester House, Kingston Hill [79, Wimpole street].

1883 BEALE, EDWIN CLIFFORD, M.A., M.B., Physician to the City of London Hospital for Diseases of the Chest, and Physician to the Great Northern Central Hospital; 23, Upper Berkeley street.

Elected

1862 BEALE, LIONEL SMITH, M.B., F.R.S., Professor of the Principles and Practice of Medicine in King's College, London, and Physician to King's College Hospital; 61, Grosvenor street. C. 1876-7. *Referee*, 1873-5. *Trans.* 1.

1897 BEDDARD, A. P., M.B., 44, Seymour street.

880 BEEVOR, CHARLES EDWARD, M.D., Physician for Out-patients to the National Hospital for the Paralysed and Epileptic, and to the Great Northern Hospital; 135, Harley street, Cavendish square. C. 1900—. *Referee*, 1896-1900. *Trans.* 1.

1901 BEEVOR, SIR HUGH REEVE, Bart., M.D., 17, Wimpole street, Cavendish square.

1877 BENNETT, SIR WILLIAM HENRY, K.C.V.O., Surgeon to St. George's Hospital; 1, Chesterfield street, Mayfair. C. 1893-4. *Referee*, 1892-93, 1899—. *Trans.* 4.

1897 BERKELEY, COMYNS, M.B., B.C., Physician to Out-Patients, Chelsea Hospital for Women; 53, Wimpole street.

1845 **Berry**, EDWARD UNWIN, 17, Sherriff road, West Hampstead.

1885 BERRY, JAMES, B.S., Surgeon to the Royal Free Hospital, and Lecturer on Surgery at the London School of Medicine for Women; Demonstrator of Practical Surgery, St. Bartholomew's Hospital; 21, Wimpole street, Cavendish square.

1893 BIDWELL, LEONARD A., Senior Assistant Surgeon to the West London Hospital; 15, Upper Wimpole street, Cavendish square.

1856 **Bird**, WILLIAM, Consulting Surgeon to the West London Hospital; Bute House, Hammersmith.

1851 **Birkett**, JOHN, F.L.S., Consulting Surgeon to Guy's Hospital; Corresponding Member of the Société de Chirurgie of Paris; 1, Sussex gardens. L. 1856-7. S. 1863-5. C. 1867-8. T. 1870-78. V.P. 1879-80. *Referee*, 1851-5, 1866, 1869. *Sci. Com.* 1863. *Lib. Com.* 1852. *Trans.* 8.

Elected

1897 BLACKER, G. F., M.D., Obstetric Physician to University College Hospital and to the Great Northern Central Hospital; 11, Wimpole street, Cavendish square.

1901 BLAIKIE, J. BRUNTON, M.D., C.M., 22, Grosvenor street, Grosvenor square.

1883 BLAND-SUTTON, JOHN, Assistant Surgeon to the Middlesex Hospital; Surgeon to the Chelsea Hospital for Women; 48, Queen Anne street, Cavendish square. *Trans.* 6.

1865 **Blandford,** GEORGE FIELDING, M.D., Lecturer on Psychological Medicine at St. George's Hospital; 48, Wimpole street, Cavendish square. C. 1883-4. V.P. 1898—1900.

1891 BOKENHAM, THOMAS JESSOPP, 10, Devonshire street, Portland place.

1882 BOWLBY, ANTHONY ALFRED, C.M.G., Assistant Surgeon to St. Bartholomew's Hospital; 24, Manchester square. *Trans.* 8.

1870 *Bowles,* ROBERT LEAMON, M.D., 16, Upper Brook street, Grosvenor square. C. 1897-9. *Sci. Com.* 1896—. *Trans.* 3.

1886 BOXALL, ROBERT, M.D., Assistant Obstetric Physician to, and Lecturer on Practical Midwifery at, the Middlesex Hospital; 40, Portland place.

1884 BOYD, STANLEY, M.B., Surgeon to, and Lecturer on Surgery at, the Charing Cross Hospital; Surgeon to the Paddington Green Children's Hospital; Consulting Surgeon to the New Hospital for Women; 134, Harley street, Cavendish square. *Referee,* 1895—. *Trans.* 1.

1890 BRADFORD, JOHN ROSE, M.D., D.Sc., F.R.S., Physician to University College Hospital; 8, Manchester square. *Referee,* 1899—. *Trans.* 1.

1897 BRAILEY, WILLIAM ARTHUR, M.D., 11, Old Burlington street.

1899 BREMRIDGE, RICHARD HARDING, 72, Great Russell street.

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1901 BREWERTON, ELMORE WRIGHT, 45, Weymouth street, Portland place.

1890 BRINTON, ROLAND DANVERS, M.D., 8, Queen's Gate terrace.

1898 **Broadbent**, J. F. H., M.D., 35, Seymour street.

1868 **Broadbent**, SIR WILLIAM HENRY, Bart., K.C.V.O., M.D., F.R.S., LL.D., Physician in Ordinary to H.M. the King; Consulting Physician to St. Mary's Hospital; Consulting Physician to the London Fever Hospital; 84, Brook street, Grosvenor square. C. 1885. *Referee*, 1881-4, 1891-7. *Trans.* 5.

1872 BRODIE, GEORGE BERNARD, M.D., Consulting Physician-Accoucheur to Queen Charlotte's Hospital; 8, Carlos place, Grosvenor square. *Trans.* 1.

1900 BROWN, WALTER LANGDON, M.D., 30, New Cavendish street, Portland place.

1880 BROWNE, JAMES WILLIAM, M.B., 37, Holland Park avenue. C. 1900-1.

1881 BROWNE, OSWALD AUCHINLECK, M.A., M.D., Physician to the Royal Hospital for Diseases of the Chest and to the Metropolitan Hospital; 7, Upper Wimpole street.

1874 BRUCE, JOHN MITCHELL, M.D., Physician to, and Lecturer on Medicine at, the Charing Cross Hospital; Consulting Physician to the Hospital for Consumption, Brompton; 23, Harley street. C. 1892, 1897-9. S. 1893-6. *Sci. Com.* 1889—. *Ho. Com.* 1898-9. *Referee*, 1886-91. *Lib. Com.* 1888-91. *Trans.* 3.

1898 BRUCE, SAMUEL NOBLE, 15, Queensborough terrace, Hyde Park.

1871 BRUNTON, SIR THOMAS LAUDER, M.D., D.Sc. LL.D., F.R.S., Physician to, and Lecturer on Pharmacology and Therapeutics at, St. Bartholomew's Hospital; 10, Stratford place, Oxford street. C. 1888-9. *Referee*, 1880-87. *Lib. Com.* 1882-7. *Trans.* 2.

Elected

1898 BRYANT, J. H., M.D., Assistant Physician to Guy's Hospital; 4, St. Thomas's street, London bridge.

1860 **Bryant**, THOMAS, M.Ch., Honorary Surgeon-in-Ordinary to H.M. the King, Consulting Surgeon to Guy's Hospital; Member of the Société de Chirurgie, Paris; 27, Grosvenor street, Grosvenor square. P. 1898-1900. C. 1873-4. V.P. 1885-6. *Sci. Com.* 1863. *Referee*, 1882-4. *Lib. Com.* 1868-71. *Trans.* 15. *Pro.* 1.

1901 BUCKNALL, THOMAS RUPERT HAMPDEN, M.S., M.D.; 35, Harley street, Cavendish square.

1889 BULL, WILLIAM CHARLES, M.B., Aural Surgeon to, and Lecturer on Aural Surgery at, St. George's Hospital; 5, Clarges street, Piccadilly.

1893 BURGHARD, FRÉDÉRIC FRANÇOIS, M.D., M.S., Surgeon to King's College Hospital and Paddington Green Children's Hospital; 86, Harley street, Cavendish square.

1885 BUTLER-SMYTHE, ALBERT CHARLES, Senior Out-Patient Surgeon, Samaritan Free Hospital for Women and Children, Soho; Senior Surgeon to the Grosvenor Hospital for Women and Children; 76, Brook street, Grosvenor square.

1873 **Butlin**, HENRY TRENTHAM, D.C.L., Surgeon to St. Bartholomew's Hospital; 82, Harley street, Cavendish square. C. 1887-8. *Referee*, 1893—. *Trans.* 4. *Pro.* 1.

1896 BUTTAR, CHARLES, M.D., 10, Kensington gardens square, Bayswater. *Pro.* 1.

1883 BUXTON, DUDLEY WILMOT, M.D., B.S., Administrator, and Teacher of the Use, of Anæsthetics, in University College Hospital; Consulting Anæsthetist to the National Hospital for the Paralysed and Epileptic, Queen square, and Anæsthetist to the London Dental Hospital; 82, Mortimer street, Cavendish square.

1899 BUZZARD, EDWARD FARQUHAR, M.B., 33, Harley street, Cavendish square.

Elected

1868 **Buzzard,** THOMAS, M,D., Physician to the National Hospital for the Paralysed and Epileptic; 74, Grosvenor street, Grosvenor square. C. 1885-6. *Referee*, 1887—.

1885 CAHILL, JOHN, M.D., Surgeon to the Hospital of St. John and St. Elizabeth; 12, Seville street, Lowndes square.

1893 CALEY, HENRY ALBERT, M.D., Physician in charge of Out-patients, Lecturer on Materia Medica and Therapeutics, and Dean of the Medical School, St. Mary's Hospital; 24, Upper Berkeley street, Portman square.

1887 CALVERT, JAMES, M.D., The Warden's House, St. Bartholomew's Hospital. *Trans.* 1.

1897 CANTLIE, JAMES, M.B., 46, Devonshire street.

1888 CARLESS, ALBERT, M.S., Assistant Surgeon to King's College Hospital; 10, Welbeck street.

1896 CARR, J. WALTER, M.D., Assistant Physician to the Royal Free Hospital; 19, Cavendish place. *Trans.* 1.

1898 CARTER, H. RONALD, 11, Leonard place, Kensington.

1853 CARTER, ROBERT BRUDENELL, Consulting Ophthalmic Surgeon to St. George's Hospital; 31, Harley street, Cavendish square, and Kenilworth, Clapham common. *Trans.* 1.

1888 CAUTLEY, EDMUND, M.D., B.C., 15, Upper Brook street, *Trans.* 1.

1871 **Cayley,** WILLIAM, M.D., Physician to the Middlesex Hospital, Consulting Physician to the London Fever Hospital, and to the North-Eastern Hospital for Children; 27, Wimpole street, Cavendish square. C. 1888. *Referee*, 1886-7, 1899—. *Lib. Com.* 1886-7. *Trans.* 2.

1879 CHAMPNEYS, FRANCIS HENRY, M.D., Physician-Accoucheur and Lecturer on Obstetric Medicine at St. Bartholomew's Hospital; 42, Upper Brook street, Grosvenor square. C. 1898-1900. *Referee*, 1891-8. *Lib. Com.* 1885-98. *Trans.* 8.

Elected

1868 **Cheadle,** WALTER BUTLER, M.D., *Trustee;* Physician to, and Lecturer on Clinical Medicine at, St. Mary's Hospital; Consulting Physician to the Hospital for Sick Children; 19, Portman street, Portman square. S. 1886-8. C. 1890-91. *Sci. Com.* 1889-95. *Bldg. Com.* 1889-92. *Referee,* 1885. *Trans.* 1.

1879 CHEYNE, WILLIAM WATSON, M.B., F.R.S., Surgeon to King's College Hospital, and Professor of Surgery in King's College, London; 75, Harley street, Cavendish square. C. 1897-9. *Referee,* 1894-7. *Lib. Com.* 1886-8, 1891-6. *Trans.* 1.

1890 CHILDS, CHRISTOPHER, M.D., 10, Manchester square.

1896 CHRISTOPHERSON, JOHN BRIAN, M.D., B.C., Assistant Demonstrator of Anatomy at St. Bartholomew's Hospital; Surgeon to Seamen's Hospital, Albert Dock; 3, Staple inn, Holborn.

1866 **Church,** SIR WILLIAM SELBY, Bart., M.D., *Hon. Treasurer,* President of the Royal College of Physicians of London, Physician to, and Lecturer on Clinical Medicine at, St. Bartholomew's Hospital; 130, Harley street, Cavendish square. C. 1885-6. V.P. 1892-4. T. 1894—. *Referee,* 1874-81. *Ho. Com.* 1898—.

1879 CLARK, ANDREW, Surgeon to, and Lecturer on Surgery at, the Middlesex Hospital; 71, Harley street, Cavendish square.

1882 CLARKE, ERNEST, M.D., B.S., Surgeon to the Central London Ophthalmic Hospital; Ophthalmic Surgeon to the Miller Hospital; 3, Chandos street, Cavendish square.

1890 CLARKE, JAMES JACKSON, M.B., Assistant Surgeon to the North-West London and City Orthopædic Hospitals; 18, Portland Place.

1848 **Clarke,** JOHN, M.D., 42, Carlisle place, Victoria street. C. 1866.

1888 CLARKE, ROBERT HENRY, M.B., 80, Hamlet Gardens, Ravenscourt Park.

Elected

1881 CLARKE, W. BRUCE, M.B., Assistant Surgeon to, and Lecturer on Anatomy at, St. Bartholomew's Hospital; Surgeon to the West London Hospital; 51, Harley street, Cavendish square. C. 1899—1901. *Trans.* 1.

1879 **Clutton,** HENRY HUGH, M.B., M.C., Surgeon to St. Thomas's Hospital; 2, Portland place. C. 1897-9. *Dis. Com.* 1897-8. *Referee*, 1896-7. *Trans.* 3.

1888 COCK, FREDERICK WILLIAM, M.D., 1, Porchester Houses, Porchester square.

1897 COLMAN, W. S., M.D., Assistant Physician to St. Thomas's Hospital; 22, Wimpole street.

1865 COOPER, ALFRED, Surgeon in Ordinary to H.R.H. the Duke of Saxe-Coburg-Gotha; Consulting Surgeon to the West London Hospital and to St. Mark's Hospital; 9, Henrietta street, Cavendish square.

1898 CORFIELD, W. H., M.D., Professor of Hygiene and Public Health at University College, London; Medical Officer of Health for St. George's, Hanover square; 19, Savile row, and Whindown, Bexhill, Sussex.

1889 COSENS, CHARLES HENRY, 49, Oxford terrace, Hyde Park.

1860 **Couper,** JOHN, Consulting Surgeon to the Royal London Ophthalmic Hospital and to the London Hospital; 80, Grosvenor street. C. 1876. *Referee*, 1882-3.

1877 COUPLAND, SIDNEY, M.D., Commissioner in Lunacy; late Physician to, and Lecturer on Medicine at, the Middlesex Hospital; 16, Queen Anne street, Cavendish square. C. 1893-4. *Referee*, 1892-3. *Ho. Com.* 1895-8.

1862 **Cowell,** GEORGE, Consulting Surgeon to the Westminster Hospital and to the Royal Westminster Ophthalmic Hospital; 19, Harley street, Cavendish square. C. 1882-3.

1897 CRAWFURD, RAYMOND H. PAYNE, M.D., 71, Harley street.

Elected

1878 CRICHTON-BROWNE, SIR JAMES, M.D., LL.D., F.R.S., Lord Chancellor's Visitor in Lunacy; 61, Carlisle place Mansions, Victoria street.

1874 CRIPPS, WILLIAM HARRISON, Surgeon to St. Bartholomew's Hospital; 2, Stratford place, Oxford street. C. 1890-91. *Trans.* 1.

1882 CROCKER, HENRY RADCLIFFE, M.D., Physician to the Skin Department, University College Hospital; 121, Harley street, Cavendish square. *Trans.* 3.

1898 CROMBIE, ALEXANDER, M.D., 3, Bickenhall Mansions, Gloucester place.

1899 CROSSE, W. H., M.D., 45, Dover street, Piccadilly.

1890 CROWLE, THOMAS HENRY RICKARD, 35, St. James's place.

1888 CULLINGWORTH, CHARLES JAMES, M.D., D.C.L., Obstetric Physician and Lecturer on Diseases of Women to St. Thomas's Hospital; 14, Manchester square. *Referee*, 1896—.

1879 CUMBERBATCH, A. ELKIN, M.B., Aural Surgeon to St. Bartholomew's Hospital, and to the National Hospital for the Paralysed and Epileptic; 80, Portland place. *Trans.* 1.

1873 CURNOW, JOHN, M.D., Professor of Clinical Medicine in King's College, London, and Physician to King's College Hospital; Senior Physician to the Seamen's Hospital; 9, Wimpole street, Cavendish square. *Referee*, 1884-97.

1898 CURRIE, A. STARK, M.D., 81, Queen's road, Finsbury park.

1886 DAKIN, WILLIAM RADFORD, M.D., Obstetric Physician to, and Lecturer in Midwifery at, St. George's Hospital, and Physician to the General Lying-in Hospital; 8, Grosvenor street, Grosvenor square.

1872 DALBY, SIR WILLIAM BARTLETT, M.B., Consulting Aural Surgeon to St. George's Hospital; 18, Savile row. C. 1896-7. V.P. 1901. *Trans.* 4.

Elected

1891 DALTON, NORMAN, M.D., Physician to King's College Hospital; Professor of Pathological Anatomy in King's College, London; 4, Mansfield street, Cavendish square.

1895 DAUBER, JOHN HENRY, M.B., B.Ch., Assistant Physician to the Hospital for Women, Soho square; 29, Charles street, Berkeley square.

1889 DEAN, HENRY PERCY, M.S., Surgeon to the London Hospital; 69, Harley street, Cavendish square.

1878 DENT, CLINTON THOMAS, *Hon. Secretary*, Surgeon to, and Lecturer on Surgery at, St. George's Hospital; 61, Brook street. C. 1890. S. 1901. *Bldg. Com.* 1890-2. *Referee*, 1892—1901. *Trans.* 6.

1891 DE SANTI, PHILIP ROBERT WILLIAM, Assistant Surgeon and Aural Surgeon to the Westminster Hospital; 15, Stratford place.

1894 DICKINSON, THOMAS VINCENT, M.D., Physician to the Italian Hospital, Queen square; 33, Sloane street.

1859 **Dickinson**, WILLIAM HOWSHIP, M.D., Consulting Physician to St. George's Hospital, and Consulting Physician to the Hospital for Sick Children; Honorary Fellow of Caius College, Cambridge; 9, Chesterfield street, Mayfair. P. 1896-8. C. 1874-5. V. P. 1887. *Referee*, 1869-73. 1882-6. *Sci. Com.* 1867, 1879, 1889-96. *Trans.* 16.

1891 **Dickinson**, WILLIAM LEE, M.D., Assistant Physician to St. George's Hospital and to the Hospital for Sick Children; 9, Chesterfield street, Mayfair.

1889 DODD, HENRY WORK, Surgeon to the Royal Westminster Ophthalmic Hospital; Ophthalmic Surgeon to the Royal Free Hospital and to the West-End Hospital for Nervous Diseases; 136, Harley street, Cavendish square.

Elected

1888 DONELAN, JAMES, M.B., M.C., Physician to the Italian Hospital, Queen square; 6, Manchester square.

1877 DORAN, ALBAN HENRY GRIFFITHS, Surgeon to the Samaritan Free Hospital; 9, Granville place, Portman square. C. 1893-4. *Lib. Com.* 1891-3, 1899—. *Referee*, 1898—. *Trans.* 3.

1899 DOUGLAS, ARCHIBALD ROBERT JOHN, M.B., B.S., 30A, Wimpole street, Cavendish square.

1891 DOVE, PERCY W., M.B., 80, Crouch hill.

1896 DOWNES, JOSEPH LOCKHART, M.B., C.M., 269, Romford road.

1893 DRYSDALE, JOHN H., M.B., 11, Devonshire place.

1865 **Duckworth**, SIR DYCE, M.D., LL.D., Physician to, and Lecturer on Medicine at, St. Bartholomew's Hospital; 11, Grafton street, Bond street. C. 1883-4. *Referee* 1885-97. *Trans.* 2.

1876 DUDLEY, WILLIAM LEWIS, M.D., Senior Physician to the City Dispensary; 149, Cromwell road, South Kensington.

1880 DUNBAR, JAMES JOHN MACWHIRTER, M.D., Hedingham House, Clapham Common.

1884 DUNCAN, WILLIAM, M.D., Obstetric Physician to, and Lecturer on Midwifery at, the Middlesex Hospital; 6, Harley street, Cavendish square.

1887 DUNN, HUGH PERCY, Ophthalmic Surgeon to the West London Hospital; 54, Wimpole street, Cavendish square.

1898 DUNN, L. A., M.S., The College, Guy's Hospital.

1874 DURHAM, FREDERIC, M.B., Senior Surgeon to the North-West London Hospital; 52, Brook street, Grosvenor square.

Elected

1894 DURHAM, HERBERT EDWARD, M.B., 52, Brook street, Grosvenor square. *Trans.* 2.

1868 **Eastes,** GEORGE, M.B.Lond., 35, Gloucester terrace, Hyde Park. C. 1892-3.

1893 ECCLES, WILLIAM MCADAM, M.S., Assistant Surgeon to the West London Hospital and to the City of London Truss Society; 124, Harley street.

1891 EDDOWES, ALFRED, M.D., 28, Wimpole street.

1898 EDKINS, J. S., 4, Park hill road, Hampstead.

1898 EDMUNDS, P. J., M.B., 5, Great Marlborough street, Regent street.

1883 EDMUNDS, WALTER, M.C., 2, Devonshire place, Portland place. *Trans.* 3.

1884 EDWARDS, FREDERICK SWINFORD, Surgeon to the West London Hospital, and to St. Peter's Hospital; Senior Assistant Surgeon to St. Mark's Hospital; 55, Harley street, Cavendish square.

1898 EVANS, WILLMOTT H., M.D., B.S., B.Sc., Assistant Surgeon and Surgeon in charge of Skin Department, Royal Free Hospital; 2, Upper Wimpole street.

1879 EVE, FREDERIC S., Surgeon to the London Hospital; Surgeon to the Evelina Hospital for Sick Children; 125, Harley street, Cavendish square. C. 1897-9. *Trans.* 4.

1877 EWART, WILLIAM, M.D., Physician to St. George's Hospital and to the Belgrave Hospital for Children; 33, Curzon street, Mayfair. C. 1895-7. *Lib. Com.* 1897—. *Sci. Com.* 1889—. *Trans.* 1. *Pro.* 1.

1900 FAIRBAIRN, JOHN SHIELDS, M.B., 60, Wimpole street.

Elected

1872 FAYRER, SIR JOSEPH, Bart., K.C.S.I., LL.D., M.D., F.R.S., Surgeon-General; Physician Extraordinary to H.M. the King; late Physician to the Secretary of State for India in Council, and President of the Medical Board at the India Office; 16, Devonshire street, Portland place. C. 1888. *Referee*, 1881-7.

1898 FENWICK, E. HURRY, Surgeon to the London Hospita and to St. Peter's Hospital; 14, Savile row.

1863 **Fenwick**, SAMUEL, M.D., Consulting Physician to the London Hospital; 29, Harley street, Cavendish square. C. 1880. *Referee*, 1882-96. *Trans.* 4.

1880 FERRIER, DAVID, M.D., LL.D., F.R.S., Professor of Neuropathology in King's College, London, and Physician to King's College Hospital; Physician to the National Hospital for the Paralysed and Epileptic; 34, Cavendish square. *Referee*, 1891-6. C. 1896-8. *Dis. Com.* 1896—. *Trans.* 2.

1889 FIELD, GEORGE P., Aural Surgeon to, and Lecturer on Aural Surgery at, St. Mary's Hospital; 34, Wimpole street, Cavendish square.

1900 FLEMMING, PERCY, M.D., B.S., Assistant Ophthalmic Surgeon to University College Hospital; Assistant Surgeon to the Royal London Ophthalmic Hospital, City road; 31, Wimpole street.

1891 FLETCHER, HERBERT MORLEY, M.D., Assistant Physician, East London Hospital for Children; 98, Harley street, Cavendish square.

1892 FORSBROOK, WILLIAM HENRY RUSSELL, M.D., 139, Buckingham Palace road.

1896 FOULERTON, ALEXANDER GRANT RUSSELL, 15A, Porchester gardens. *Trans.* 1.

1883 FOWLER, JAMES KINGSTON, M.D., Physician to, and Lecturer on Medicine at, the Middlesex Hospital; Physician to the Hospital for Consumption, Brompton, 35, Clarges street, Piccadilly. *Trans.* 1.

Elected

1880 FOX, THOMAS COLCOTT, B.A., M.B., Physician for Diseases of the Skin to the Westminster Hospital, and Physician to the Skin Department of the Paddington Green Hospital for Children; 14, Harley street, Cavendish square. *Trans.* 1.

1871 FRANK, PHILIP, M.D., 3, Elvaston place, South Kensington.

1896 FREYER, P. J., M.D., M.Ch., Surgeon to St. Peter's Hospital; 46, Harley street, Cavendish square. *Trans.* 1.

1898 FRIPP, A. DOWNING, C.B., M.V.O., M.S., Honorary Surgeon in Ordinary to H.M. the King; Assistant Surgeon to Guy's Hospital; 19, Portland place.

1898 FROST, WILLIAM ADAMS, Ophthalmic Surgeon to St. George's Hospital, and Surgeon to Royal Westminster Ophthalmic Hospital; 30, Cavendish square.

1899 FÜRTH, KARL, M.D., 92, Harley Street.

1884 FULLER, CHARLES CHINNER, 10, St. Andrew's place, Regent's Park.

1883 FULLER, HENRY ROXBURGH, M.D., 45, Curzon street, Mayfair.

1894 FURNIVALL, PERCY, Assistant Surgeon, London Hospital; Assistant Surgeon, St. Mark's Hospital; 28, Weymouth street, Portland place.

1874 **Galabin**, ALFRED LEWIS, M.D., Obstetric Physician to, and Lecturer on Midwifery and the Diseases of Women at, Guy's Hospital; 49, Wimpole st., Cavendish square. C. 1892. *Referee*, 1882-91, 1896—. *Lib. Com.* 1883-4. *Trans.* 2.

1895 GALLOWAY, JAMES, M.D., Physician, Skin Department, and Joint Lecturer on Practical Medicine, Charing Cross Hospital; 54, Harley street, Cavendish square.

1883 GALTON, JOHN CHARLES, M.A., F.L.S., 10, Upper Cheyne row, Chelsea.

1865 **Gant**, FREDERICK JAMES, Consulting Surgeon to the Royal Free Hospital; 16, Connaught square, Hyde Park. C. 1880-81. V.P. 1897-9. *Referee*, 1886-97. *Lib. Com.* 1882-5. *Trans.* 3.

Elected

1854 **Garrod**, Sir Alfred Baring, M.D., F.R.S., Physician Extraordinary to Her late Majesty Queen Victoria; Consulting Physician to King's College Hospital; 10, Harley street, Cavendish square. C. 1867. V.P. 1880-81. *Referee*, 1855-65. *Trans.* 9.

1886 Garrod, Archibald Edward, M.D., Medical Registrar and Demonstrator of Morbid Anatomy, St. Bartholomew's Hospital; Physician to the Hospital for Sick Children, Great Ormond street; 9, Chandos street, Cavendish square. *Sci. Com.* 1889—. *Lib. Com.* 1896—. *Trans.* 6.

1887 Gay, John, 119, Upper Richmond road, Putney.

1866 **Gee**, Samuel Jones, M.D., *Chairman of Trustees for Debenture-holders;* Honorary Physician to H.R.H. the Prince of Wales; Physician to St. Bartholomew's Hospital; 31, Upper Brook street, Grosvenor square. C. 1883-4. L. (June) 1887-99. V.P. 1899-1900. *Sci. Com.* 1879. *Bldg. Com.* 1889-92. *Referee*, 1885-7, 1900—. *Lib. Com.* 1871-6. *Ho. Com.* 1898-1900. *Trans.* 1.

1885 Gell, Henry Willingham, M.B., 36, Hyde Park square.

1898 Gibbes, Cuthbert Chapman, M.D., 89, Harley street.

1880 Gibbons, Robert Alexander, M.D., Physician to the Grosvenor Hospital for Women and Children; 29, Cadogan place. C. 1896-7. *Trans.* 1.

1893 Giles, Arthur Edward, M.D., B.Sc., Assistant Surgeon, Chelsea Hospital for Women; 10, Upper Wimpole street.

1894 Gill, Richard, 72, Wimpole street.

1877 Godlee, Rickman John, M.S., *Hon. Librarian;* Honorary Surgeon-in-Ordinary to H.M. the King; Surgeon to University College Hospital, and Professor of Clinical Surgery in University College, London; Surgeon to the Hospital for Consumption, Brompton; 19, Wimpole street, Cavendish square. S. 1892-4. L. 1895—. *Referee*, 1886-91. *Ho. Com.* 1898—. *Trans.* 10.

Elected

1870 **Godson**, CLEMENT, M.D., Consulting Physician to the City of London Lying-in Hospital; 82, Brook street, Grosvenor square.

1886 GOLDING-BIRD, CUTHBERT HILTON, M.B., Surgeon to, and Lecturer on Clinical Surgery at, Guy's Hospital; 12, Queen Anne street, Cavendish square. *Trans.* 1.

1897 GOODBODY, F. W., M.D., 6, Chandos street, Cavendish square.

1896 GOODALL, EDWARD WILBERFORCE, M.D., B.S., Eastern Hospital, Homerton.

1883 GOODHART, JAMES FREDERIC, M.D., Physician to Guy's Hospital; Consulting Physician to the Evelina Hospital for Sick Children; 25, Portland place. *Referee*, 1900—. *Lib. Com.* 1893-6.

1889 GOODSALL, DAVID HENRY, Surgeon to the Metropolitan Hospital; Surgeon to St. Mark's Hospital; 17, Devonshire place, Upper Wimpole street.

1895 GOSSAGE, ALFRED MILNE, M.B., 54, Upper Berkeley street.

1877 GOULD, ALFRED PEARCE, M.S., Surgeon to, and Lecturer on Surgical Pathology at, the Middlesex Hospital; 10, Queen Anne street, Cavendish square. C. 1892-3. S. 1898—1901. *Referee*, 1895-8. *Ho. Com.* 1892-8. *Lib. Com.* 1891. *Trans.* 3.

1891 GOW, WILLIAM J., M.D., Assistant Obstetric Physician to St. Mary's Hospital; Obstetric Physician to the Royal Hospital for Women and Children; Physician to Out-Patients, Queen Charlotte's Lying-in Hospital; 27, Weymouth street, Portland place.

1873 **Gowers**, SIR WILLIAM RICHARD, M.D., F.R.S., Consulting Physician to University College Hospital; Physician to the National Hospital for the Paralysed and Epileptic; 50, Queen Anne street, Cavendish square. C. 1891. *Referee* 1888-90. *Lib. Com.* 1884-6. *Trans.* 7.

1892 GRANT, J. DUNDAS, M.A., M.D., 18, Cavendish square.

Elected

1898 GRANVILLE, ALEXANDER, St. Bartholomew's Hospital.

1868 GREEN, T. HENRY, M.D., Physician to the Charing Cross Hospital, and to the Hospital for Consumption, Brompton; 74, Wimpole street, Cavendish square. C. 1886. *Referee*, 1882-5.

1885 GRIFFITH, WALTER SPENCER ANDERSON, M.D., Assistant Physician-Accoucheur, St. Bartholomew's Hospital; Physician to Queen Charlotte's Lying-in Hospital; 96, Harley street, Cavendish square.

1889 GUBB, ALFRED S., M.D., 29, Gower street.

1883 GUNN, ROBERT MARCUS, M.B., Surgeon to the Royal London Ophthalmic Hospital, Moorfields; Ophthalmic Surgeon to the National Hospital for the Paralysed and Epileptic; 54, Queen Anne street, Cavendish square.

1890 GUTHRIE, LEONARD GEORGE, M.D., B.Ch., Physician to the Regent's Park Hospital for Epilepsy and Paralysis; Assistant Physician to the North-West London Hospital; Assistant Physician to the Children's Hospital, Paddington Green; 15, Upper Berkeley street, Portman square.

1886 HABERSHON, SAMUEL HERBERT, M.D., Assistant Physician to the Hospital for Consumption, Brompton; 88, Harley street, Cavendish square.

1885 HAIG, ALEXANDER, M.D., Physician to the Metropolitan Hospital, and to the Royal Hospital for Children and Women; 7, Brook street, Grosvenor square. *Trans.* 6.

1890 HALE, CHARLES DOUGLAS BOWDICH, M.D., 3, Sussex place, Hyde Park.

1881 Hall, FRANCIS DE HAVILLAND, M.D., Physician to, and Joint Lecturer on Medicine at, the Westminster Hospital; Physician to St. Mark's Hospital; 47, Wimpole street, Cavendish square. C. 1901. *Referee*, 1893-7.

Elected

1891 HAMER, WILLIAM HEATON, M.D., Ardeevin, 73, Dartmouth Park Hill, Highgate.

1889 HANDFIELD-JONES, MONTAGU, M.D., Obstetric Physician to, and Lecturer on Midwifery and Diseases of Women at, St. Mary's Hospital; Physician to the British Lying-in Hospital; 35, Cavendish square.

1893 HARLEY, VAUGHAN, M.D., 25, Harley street, Cavendish square.

1901 HARMER, WILLIAM DOUGLAS, M.B., St. Bartholomew's Hospital.

1892 HAROLD, JOHN, 91, Harley street, Cavendish square.

1880 HARRIS, VINCENT DORMER, M.D., Physician to the City of London Hospital for Diseases of the Chest, Victoria Park; 22, Queen Anne street, Cavendish square. *Referee*, 1899—.

1870 HARRISON, REGINALD, Surgeon to St. Peter's Hospital; 6, Lower Berkeley street, Portman square. C. 1894-5. V.-P. 1898-1900. *Trans.* 3.

1870 **Haward**, J. WARRINGTON, *Hon. Treasurer;* Surgeon to, and Lecturer on Clinical Surgery at, St. George's Hospital; 57, Green street, Grosvenor Square. C. 1885. S. 1888-91. V.P. 1894-5. T. (June) 1895—. *Lib. Com.* 1881-4. *Sci. Com.* 1889-91. *Bldg. Com.* (*Sec.*) 1889-92. *Ho. Com.* 1892—. *Trans.* 3.

1891 HAWKINS, HERBERT PENNELL, M.D., B.Ch., Physician to St. Thomas's Hospital; 56, Portland place.

1875 HAYES, THOMAS CRAWFORD, M.D., Physician-Accoucheur and Physician for Diseases of Women and Children to King's College Hospital, and Professor of Midwifery in King's College; Physician for Diseases of Women to the Royal Free Hospital; 17, Clarges street, Piccadilly.

1891 HAYWARD, JOHN ARTHUR, M.D., 17, Lingfield road, Wimbledon. *Pro.* 1.

Elected

1865 **Heath,** CHRISTOPHER, Emeritus Professor of Clinical Surgery in University College, London; and Consulting Surgeon to University College Hospital; 36, Cavendish square. C. 1880. V.P. 1889. *Lib. Com.* 1870-3. *Trans.* 3.

1895 HENDERSON, EDWARD ERSKINE, B.A., M.B., B.C., 20, Queen Anne street, Cavendish square.

1901 HENRY, JOHN PATRICK, M.D., B.Ch., 41, Welbeck street, Cavendish square.

1882 HENSLEY, PHILIP JOHN, M.D., Physician to, and Lecturer on Forensic Medicine at, St. Bartholomew's Hospital; 4, Henrietta street, Cavendish square. *Referee*, 1897—.

1877 HERMAN, GEORGE ERNEST, M.B., Obstetric Physician to, and Lecturer on Midwifery at, the London Hospital; 20, Harley street, Cavendish square. C. 1900—. *Referee*, 1892-1900. *Lib. Com.* 1898-1900. *Trans.* 1.

1900 HERN, WILLIAM, 7, Stratford place.

1877 HERON, GEORGE ALLAN, M.D., Physician to the City of London Hospital for Diseases of the Chest, Victoria Park; 57, Harley street, Cavendish square.

1891 HERRING, HERBERT T., M.B., B.S., 50, Harley street, Cavendish square.

1883 HERRINGHAM, WILMOT PARKER, M.D., Assistant Physician, St. Bartholomew's Hospital; 40, Wimpole street, Cavendish square. *Trans.* 2.

1893 HERSCHELL, GEORGE, M.D., 76, Wimpole street, Cavendish square.

1887 HEWITT, FREDERIC WILLIAM, M.D., Honorary Anæsthetist to H.M. the King; Anæsthetist to, and Instructor in Anæsthetics at, the London Hospital; Anæsthetist at the Dental Hospital of London; 14, Queen Anne street, Cavendish square. *Trans.* 3.

Elected

1873 HIGGENS, CHARLES, Ophthalmic Surgeon to, and Lecturer on Ophthalmic Surgery at, Guy's Hospital; 52, Brook street, Grosvenor square. C. 1894-5. *Trans.* 2.

1890 HILL, G. WILLIAM, M.D., B.Sc., 26, Weymouth street, Portland place.

1899 HILLIER, ALFRED P., M.D., 30, Wimpole street.

1856 **Holmes**, TIMOTHY, M.A., Consulting Surgeon to St. George's Hospital; Corresponding Member of the Société de Chirurgie, Paris; 6, Sussex place, Hyde Park. C. 1869-70. L. 1873-7. S. 1878-80. V.P. 1881-2. T. 1885-7. P. 1890-92. *Bldg.Com.* (*Chairman*) 1889-92. *Referee*, 1866-8, 1872, 1883-4. *Sci. Com.* 1867. *Lib. Com.* 1863-5, 1892-5. *Ho. Com.* 1892-8. *Trans.* 8.

1878 HOOD, DONALD WILLIAM CHARLES, C.V.O., M.D., Senior Physician to the West London Hospital; Examining Physician for Queen's Messengers, Foreign Office; 43, Green street, Park lane.

1898 HORDER, THOMAS J., M.D., 141, Harley Street.

1883 HORSLEY, VICTOR ALEXANDER HADEN, F.R.S., Surgeon to University College Hospital, Surgeon to the National Hospital for the Paralysed and Epileptic; 25, Cavendish square. *Referee*, 1897—. *Trans.* 1.

1896 HORTON-SMITH, PERCIVAL, M.D., 15, Upper Brook street. *Sci. Com.* 1897—. *Trans.* 1.

1892 HOWARD, R. J. BLISS, M.D., 31, Queen Anne street, Cavendish square.

1874 HOWSE, HENRY GREENWAY, M.S., Surgeon to, and Lecturer on Surgery at, Guy's Hospital; Consulting Surgeon to the Evelina Hospital for Sick Children; 59, Brook street, Grosvenor square. C. 1890. V.P. 1899—1901. *Sci. Com.* 1879. *Referee*, 1887-89. *Trans.* 3.

Elected

1889 HUNTER, WILLIAM, M.D., Senior Assistant Physician to the London Fever Hospital; Curator and Pathologist, Charing Cross Hospital; 103, Harley street.

1873 HUNTER, SIR W. GUYER, M.D., K.C.M.G., Surgeon-General (Retired) Bombay Army; Consulting Physician to Charing Cross Hospital.

1856 **Hutchinson**, JONATHAN, F.R.S., Consulting Surgeon to, and Emeritus Professor of Surgery at, the London Hospital; Consulting Surgeon to the Royal London Ophthalmic Hospital, Moorfields; and Senior Surgeon to the Hospital for Diseases of the Skin; 15, Cavendish square. C. 1870. V.P. 1882. P. 1894-5. *Referee*, 1876-81, 1883-94. *Lib. Com.* 1864-5. *Trans.* 14. *Pro.* 2.

1888 HUTCHINSON, JONATHAN, Jun., Surgeon to the London Hospital; 1, Park crescent. *Trans.* 3.

1897 HUTCHISON, ROBERT, M.D., 25, Welbeck street, Cavendish square.

1871 JACKSON, J. HUGHLINGS, M.D., LL.D., F.R.S., Consulting Physician to the London Hospital; Physician to the National Hospital for the Paralysed and Epileptic; 3, Manchester square. C. 1889.

1883 JACOBSON, WALTER HAMILTON ACLAND, M.Ch.Oxon., Assistant Surgeon to Guy's Hospital; Surgeon to the Royal Hospital for Children and Women; 66, Great Cumberland place, Hyde Park. *Referee*, 1895—. *Lib. Com.* 1896—. *Trans.* 2.

1892 JAMES, EDWIN MATTHEWS, Belgrave Mansions, Grosvenor gardens, and Pavilion, Melrose, N.B.

1897 JENNER, LOUIS, M.B., 4A, Bloomsbury square.

1883 JESSOP, WALTER H. H., M.B., Ophthalmic Surgeon to St. Bartholomew's Hospital; 73, Harley street. *Referee*, 1901.

Elected

1881 JOHNSON, GEORGE LINDSAY, M.D., Cortina, Netherhall gardens, South Hampstead, and 36, Finsbury pavement.

1889 JOHNSON, RAYMOND, M.B., B.S., Assistant Surgeon to University College Hospital; Surgeon to the Victoria Hospital for Children; 11, Wimpole street, Cavendish square. *Trans.* 1.

1884 JOHNSTON, JAMES, M.D., 53, Prince's square, Bayswater.

1899 **Jones**, GEORGE, M.B., 8, Church terrace, Lee.

1887 JONES, HENRY LEWIS, M.D., Medical Officer in charge of Electrical Department at St. Bartholomew's Hospital; 61, Wimpole street, Cavendish square.

1896 JONES, L. VERNON, B.A., M.D., B.Ch., 7, Arlington street, St. James's.

1881 JULER, HENRY EDWARD, Ophthalmic Surgeon to St. Mary's Hospital; Surgeon to the Royal Westminster Ophthalmic Hospital; Consulting Ophthalmic Surgeon to the London Lock Hospital; 23, Cavendish square. C. 1901—.

1898 KEEP, A. CORBIE, M.D., C.M., Surgeon to out-patients Samaritan Free Hospital for Women and Children; 14, Gloucester place, Portman square.

1882 KEETLEY, CHARLES R. B., Senior Surgeon to the West London Hospital; 56, Grosvenor street, Grosvenor square. C. 1901—.

1898 KELLOCK, THOMAS HERBERT, M.D., B.C., Assistant Surgeon to Middlesex Hospital and to the Hospital for Sick Children; 8, Queen Anne street, Cavendish square.

1857 **Kiallmark**, HENRY WALTER, 5, Pembridge gardens. C. 1890–91.

1881 KIDD, PERCY, M.D., Physician to the Hospital for Consumption, Brompton; Physician to the London Hospital; 60, Brook street, Grosvenor square. C. 1900—. *Trans.* 4.

Elected

1851 **Kingdon**, JOHN ABERNETHY, Consulting Surgeon to the Bank of England, Threadneedle street. C. 1866–7. V.P. 1872–3. *Sci. Com.* 1867. *Trans.* 1.

1900 LAKE, RICHARD, 19, Harley street. *Trans.* 1.

1896 LANE, JAMES ERNEST, Surgeon to Out-patients, St. Mary's Hospital; 46, Queen Anne Street, Cavendish square.

1884 LANE, WILLIAM ARBUTHNOT, M.S., Surgeon to Guy's Hospital and to the Hospital for Sick Children, 21, Cavendish square. *Trans.* 4.

1882 LANG, WILLIAM, Ophthalmic Surgeon to, and Lecturer on Ophthalmic Surgery at, the Middlesex Hospital; Surgeon to the Royal London Ophthalmic Hospital, Moorfields; 22, Cavendish square.

1894 LANGDON-DOWN, REGINALD LANGDON, M.B., B.C., 47, Welbeck street.

1865 **Langton**, JOHN, Surgeon to, and Lecturer on Clinical Surgery at, St. Bartholomew's Hospital; Surgeon to the City of London Truss Society; 62, Harley street, Cavendish square. C. 1881–2. V.P. 1895–7. *Referee*, 1885–95. *Lib. Com.* 1879–80, 1888–95. *Trans.* 2.

1898 LATHAM, A. C., M.D., 44, Brook street, Grosvenor square.

1890 LAW, EDWARD, M.D., C.M., 35, Harley street, Cavendish square.

1898 LAWFORD, J. B., Ophthalmic Surgeon and Lecturer on Ophthalmology, St. Thomas's Hospital; Surgeon to Royal London Ophthalmic Hospital; 99, Harley street.

1888 LAWRENCE, LAURIE ASHER, 9, Upper Wimpole street.

1890 LAWRIE, EDWARD, M.B., Surgeon Lieutenant-Colonel, Indian Medical Department; late Residency Surgeon, Hyderabad, Deccan; Harley Lodge, 115A, Harley street.

Elected

1893 LAWSON, ARNOLD, Ophthalmic Surgeon to the Children's Hospital, Paddington Green; 12, Harley street, Cavendish square.

1884 LAWSON, GEORGE, Consulting Surgeon to the Royal London Ophthalmic Hospital; Consulting Surgeon to the Middlesex Hospital; 12, Harley street, Cavendish square.

1900 LEAF, CECIL HUNTINGTON, M.A., M.B.; 75, Wimpole street, Cavendish square.

1896 LEE, WILLIAM EDWARD, M.D., Santhapuram, Muswell hill road, Highgate.

1895 LEES, DAVID BRIDGE, M.D., Physician to, and Lecturer on Medicine at, St. Mary's Hospital, and Physician to the Hospital for Sick Children; 22, Weymouth street, Portland place. *Trans.* 2.

1899 LEGGE, THOMAS MORISON, M.D., 2, Mitre court buildings, Temple.

1900 LENDON, EDWIN HARDING, M.B., 162, Holland park avenue.

1895 LESLIE, ROBERT MURRAY, M.B., Assistant Physician to Royal Hospital for Diseases of the Chest; 53, Queen Anne street.

1897 LEVY, ALFRED G., M.D., 16, York place, Portman square.

1886 LEWERS, ARTHUR HAMILTON NICHOLSON, M.D., Obstetric Physician to the London Hospital; 72, Harley street, Cavendish square. *Trans.* 1.

1878 LISTER, LORD, D.C.L., LL.D., F.R.S., Sergeant-Surgeon in Ordinary to H.M. the King; Emeritus Professor of Clinical Surgery in King's College, London; and Consulting Surgeon to King's College Hospital; 12, Park crescent, Regent's Park. C. 1892.

1891 LITTLE, ERNEST MUIRHEAD, Surgeon to the National Orthopædic Hospital; 40, Seymour street, Portman square.

Elected

1889 LITTLE, JOHN FLETCHER, M.B., 32, Harley street, Cavendish square.

1881 LOCKWOOD, CHARLES BARRETT, Surgeon to the Great Northern Central Hospital; Assistant Surgeon to, and Lecturer on Surgical and Descriptive Anatomy at, St. Bartholomew's Hospital; 19, Upper Berkeley street, Portman square. C. 1901—. *Trans.* 4.

1897 LOW, HAROLD, 10, Evelyn gardens.

1881 LUCAS, RICHARD CLEMENT, B.S., M.B., Surgeon to, and Lecturer on Surgery, late Lecturer on Anatomy at, Guy's Hospital; Consulting Surgeon to the Evelina Hospital for Sick Children; 50, Wimpole street, Cavendish square. C. 1900—. *Ho. Com.* 1901—. *Trans.* 3.

1888 LUFF, ARTHUR PEARSON, M.D., B.Sc., Physician to Outpatients and Lecturer on Medical Jurisprudence at St. Mary's Hospital; 31, Weymouth street, Portland place. *Trans.* 1.

1887 LUSH, PERCY J. F., M.B., 4, Maresfield gardens, Hampstead.

1898 LYSTER, C. R. C., Bolingbroke Hospital, Wandsworth common.

1873 **MacCarthy**, JEREMIAH, M.A., Surgeon to the London Hospital, late Lecturer on Surgery at the London Hospital Medical College; 1, Cambridge place, Victoria road, Kensington. C. 1886-7. *Lib. Com.* 1882-5. *Referee*, 1890—.

1899 MACDONALD, GREVILLE, M.D., 85, Harley street.

1898 MCFADYEAN, JOHN, The Royal Veterinary College, Camden Town.

1894 MACFADYEN, ALLAN, M.D., B.S., Jenner Institute of Preventive Medicine, Chelsea bridge.

Elected

1896 MacGregor, Alexander, M.D., 8, Queen street, Mayfair.

1880 McHardy, Malcolm Macdonald, Ophthalmic Surgeon to King's College Hospital, and Professor of Ophthalmic Surgery in King's College, London; Senior Surgeon to the Royal Eye Hospital, Southwark; 5, Savile row.

1873 MacKellar, Alexander Oberlin, M.Ch., Surgeon to St. Thomas's Hospital; Surgeon-in-Chief to the Metropolitan Police Force; 79, Wimpole street, Cavendish square.

1881 Mackenzie, Stephen, M.D., Physician to the London Hospital; Physician to the Royal London Ophthalmic Hospital; 18, Cavendish square. C. 1899-1900. *Referee*, 1890-9. *Trans.* 1.

1879 Maclagan, Thomas John, M.D., Physician-in-Ordinary to their R.H. the Prince and Princess Christian of Schleswig-Holstein; 9, Cadogan place, Belgrave square.

1876 Macnamara, N. Charles, Consulting Surgeon to the Westminster Hospital, and to the Royal Westminster Ophthalmic Hospital; 21, Grosvenor street, Grosvenor square, W. C. 1891-2. *Referee*, 1884-90, 1895-7. *Lib. Com.* 1886-90.

1881 Macready, Jonathan Forster Christian Horace, Surgeon to the Great Northern Hospital; 42, Devonshire street.

1880 Maddick, Edmund Distin, 31, Cavendish square.

1886 Maguire, Robert, M.D., Physician to Out-patients and Joint Lecturer on Pathology at St. Mary's Hospital; Physician to the Hospital for Consumption, Brompton; 4, Seymour street, Portman square. *Sci. Com.* 1889—.

1880 Makins, George Henry, C.B., Surgeon to St. Thomas's Hospital; Consulting Surgeon to the Evelina Hospital for Children; 47, Charles street, Berkeley square. C. 1899-1900. *Referee*, 1898-9. *Trans.* 2.

Elected

1885 MALCOLM, JOHN DAVID, M.B., C.M., Surgeon to the Samaritan Free Hospital; 13, Portman street, Portman square. *Trans.* 2.

1890 MANSON, PATRICK, M.D., C.M., LL.D., Physician to the Seamen's Hospital, Albert Docks; Lecturer on Tropical Medicine at St. George's Hospital; 21, Queen Anne street, Cavendish square.

1867 MARSH, F. HOWARD, Surgeon to, and Lecturer on Surgery at, St. Bartholomew's Hospital; 30, Bruton street, Berkeley square. C. 1882-3, 1889. S. 1885-7. V.P. 1891-3. *Lib. Com.* 1880-1. *Trans.* 4.

1891 MARTIN, HENRY CHARRINGTON, M.D., 27, Oxford square.

1884 MARTIN, SIDNEY HARRIS COX, M.D., F.R.S., Assistant Physician to University College Hospital, and to the Hospital for Consumption, Brompton; Professor of Pathology, University College, London; 10, Mansfield street, Portland place.

1892 MASTERS, JOHN ALFRED, M.D., 31, Albert gate, Hyde Park.

1891 MAY, WILLIAM PAGE, M.D., B.Sc., 9, Manchester square.

1891 MERCIER, CHARLES ARTHUR, M.B., Lecturer on Neurology and Insanity at Westminster Hospital; 8, New Court, Lincoln's Inn, and Flower House, Southend, Catford.

1880 MEREDITH, WILLIAM APPLETON, M.B., C.M., Surgeon to the Samaritan Free Hospital for Women and Children; 21, Manchester square. C. 1897-9. *Ho. Com.* 1898-9. *Trans.* 1.

1894 MICHELS, ERNST, M.D., Surgeon to the German Hospital; 48, Finsbury square. *Trans.* 2.

1893 MILEY, MILES, M.B., 21, Belsize avenue, Hampstead.

1891 MOLINE, PAUL, M.B., 42, Walton street, Chelsea.

Elected

1873 MOORE, NORMAN, M.D., *Hon. Librarian*, Assistant Physician and Lecturer on Medicine to St. Bartholomew's Hospital; 94, Gloucester place, Portman square. C. 1891-2. L. 1899—. S. 1896-9. *Referee*, 1886-90. *Ho. Com.* 1898—. *Sci. Com.* 1889—.

1878 MORGAN, JOHN HAMMOND, C.V.O., M.A., Surgeon to the Charing Cross Hospital, and to the Hospital for Sick Children, Great Ormond street; 68, Grosvenor street. C. 1895-7. *Dis. Com.* 1896-7. *Referee*, 1901—. *Trans.* 2.

1894 MORISON, ALEXANDER, M.D., 14, Upper Berkeley street.

1874 **Morris**, HENRY, M.A., Surgeon to the Middlesex Hospital; 8, Cavendish square. C. 1888-9. V.P. 1900—. *Referee*, 1882-7. *Lib. Com.* 1895-6. *Trans.* 10.

1879 MORRIS, MALCOLM ALEXANDER, Surgeon to the Skin Department of, and Lecturer on Dermatology at, St. Mary's Hospital; 8, Harley street, Cavendish square. *Sci. Com.* 1889—. *Trans.* 1.

1898 MORRISON, JAMES, M.D., 11, Brook street, Grosvenor square.

1885 MOTT, FREDERICK WALKER, M.D., F.R.S., Assistant Physician, Charing Cross Hospital; Pathologist to the London County Council; 25, Nottingham place. *Referee*, 1900—. *Sci. Com.* 1899—. *Trans.* 1.

1900 MUIR, HENRY SKEY, Surgeon-General, C.B., M.D., R.A.M.C., Deputy-Inspector-General, Medical Department, War Office, 18, Victoria street.

1899 MUNDY, HERBERT, St. Bartholomew's Hospital.

1900 MURPHY, WILLIAM REID, D.S.O., Lieutenant-Colonel I.M.S.; Junior Army and Navy Club, 10, St. James's street.

1896 **Murphy**, JAMES KEOGH, M.B., St. Bartholomew's Hospital.

Elected

1888 **Murray**, HUBERT MONTAGUE, M.D., Physician to Out-patients, and Joint Lecturer on Medicine at, the Charing Cross Hospital; Physician to the Victoria Hospital for Children; 25, Manchester square.

1898 MURRAY, JOHN, Assistant Surgeon to the Middlesex Hospital and to the Paddington Green Children's Hospital; 110, Harley street.

1880 MURRELL, WILLIAM, M.D., Physician to, and Lecturer on Materia Medica, Pharmacology, and Therapeutics at, the Westminster Hospital; 17, Welbeck street, Cavendish square. *Sci. Com.* 1889—. *Trans.* 1.

1892 MYDDELTON-GAVEY, E. HERBERT, 124, Harley street, Cavendish square, and 16, Broadwater Down, Tunbridge Wells.

1863 **Myers**, ARTHUR BOWEN RICHARDS, late Brigade-Surgeon, Brigade of Guards; 43, Gloucester street, Warwick square. C. 1878-9. *Lib. Com.* 1877.

1864 NUNN, THOMAS WILLIAM, Consulting Surgeon to the Middlesex Hospital; 8, Stratford place, Oxford street.

1880 OGILVIE, GEORGE, M.B., B.Sc., Physician to the Hospital for Epilepsy and Paralysis, Regent's Park; 22, Welbeck street, Cavendish square. *Trans.* 1.

1891 OGLE, CYRIL, M.A., M.B., Assistant Physician to St. George's Hospital; 96, Gloucester place, Portman square.

1858 **Ogle**, JOHN WILLIAM, M.D., Consulting Physician to St. George's Hospital; 96, Gloucester place, Portman square. C. 1873. V.P. 1886. *Referee*, 1864-72. *Trans.* 4.

1860 OGLE, WILLIAM, M.D., late Superintendent of Statistics in the Registrar-General's Department, Somerset House; 10, Gordon street, Gordon square. S. 1868-70. C. 1876-7. V.P. 1887. *Lib. Com.* 1871-5. *Trans.* 5.

1892 OPENSHAW, T. HORROCKS, M.B., M.S., Surgeon to, and Lecturer on Anatomy at, the London Hospital; 16, Wimpole street, Cavendish square.

Elected

1873 ORD, WILLIAM MILLER, M.D., Consulting Physician to St. Thomas's Hospital; 37, Upper Brook street, Grosvenor square. C. 1889–90. *Sci. Com.* 1889—. *Referee*, 1884-8. *Trans.* 6.

1877 ORMEROD, JOSEPH ARDERNE, M.D., Assistant Physician to St. Bartholomew's Hospital; Physician to the National Hospital for the Paralysed and Epileptic, Queen square; 25, Upper Wimpole street. C. 1897. *Lib. Com.* 1896-7. *Trans.* 1.

1875 OSBORN, SAMUEL, 1A, Devonshire street, Portland place, and Maisonnette, Datchet, Bucks.

1879 OWEN, EDMUND, M.B., Senior Surgeon to, and Lecturer on Clinical Surgery at, St. Mary's Hospital; Senior Surgeon to the Hospital for Sick Children, Great Ormond street; 64, Great Cumberland place, Hyde park. C. 1896-7. *Trans.* 4.

1882 OWEN, ISAMBARD, M.D., Deputy-Chancellor of the University of Wales; Physician to, and Lecturer on Forensic Medicine at, St. George's Hospital; 40, Curzon street, Mayfair. *Bldg. Com.* 1889-92. *Referee*, 1893, 1895—.

1892 PAGE, H. MARMADUKE, 26, Ashley gardens, Victoria street.

1874 PAGE, HERBERT WILLIAM, M.A., M.C., Surgeon to, and Joint Lecturer on Surgery at, St. Mary's Hospital; 146, Harley street, Cavendish square. C. 1890-91. *Referee*, 1884-9. *Lib. Com.* 1886-8. *Trans.* 4.

1886 PAGET, STEPHEN, Surgeon to the West London Hospital; Surgeon to the Throat and Ear Department of the Middlesex Hospital; 70, Harley street.

1895 PARKER, CHARLES ARTHUR, 141, Harley street, Cavendish square.

1889 PARSONS, J. INGLIS, M.D., Physician to the Chelsea Hospital for Women; 3, Queen street, Mayfair.

Elected

1883 PASTEUR, WILLIAM, M.D., Senior Assistant Physician to the Middlesex Hospital; Consulting Physician to the North-Eastern Hospital for Children; 4, Chandos street, Cavendish square.

1901 PATERSON, HERBERT JOHN, 9, Upper Wimpole street.

1891 PATERSON, WILLIAM BROMFIELD, 7A, Manchester square.

1891 PATON, EDWARD PERCY, M.D., M.S., 84, Park street, Grosvenor square.

1865 **Pavy**, FREDERICK WILLIAM, M.D., LL.D., F.R.S., *President*, Consulting Physician to Guy's Hospital; 35, Grosvenor street. P. 1900—. C. 1883-4. V.P. 1893-4. *Referee*, 1871-82. *Trans.* 1.

1869 PAYNE, JOSEPH FRANK, M.D., Physician to, and Lecturer on Medicine at, St. Thomas's Hospital; 78, Wimpole street, Cavendish square. C. 1887. *Referee*, 1890—. *Sci. Com.* 1879. *Lib. Com.* 1878-85, 1889—.

1894 PEGLER, L. HEMINGTON, M.D., 2, Henrietta street, Cavendish square.

1898 PENDLEBURY, HERBERT STRINGFELLOW, M.B., B.C., 44, Brook street, Grosvenor square.

1887 PENROSE, FRANCIS GEORGE, M.D., Physician to St. George's Hospital and to the Hospital for Sick Children, Great Ormond street; 84, Wimpole street, Cavendish square. *Sci. Com.* 1889—.

1890 PERRY, EDWIN COOPER, M.D., Physician to, and Demonstrator of Pathology at, Guy's Hospital; The Superintendent's House, Guy's Hospital.

1895 PHEAR, ARTHUR G., M.D., Assistant Physician and Pathologist to the Metropolitan Hospital; 47, Weymouth street, Portland place. *Trans.* 1.

1883 PHILLIPS, CHARLES DOUGLAS F., M.D., LL.D., 10, Henrietta street, Cavendish square.

1884 PHILLIPS, GEORGE RICHARD TURNER, J.P., 28, Palace Court, Bayswater hill.

Elected

1888 PHILLIPS, JOHN, M.A., M.D., Obstetric Physician, King's College Hospital; Lecturer on Practical Obstetrics in King's College; Physician to the British Lying-in Hospital; 68, Brook street, Grosvenor square. *Trans.* 1.

1898 PHILLIPS, L. C. POWELL, Kasr-el-Aini Hospital, Cairo.

1889 PHILLIPS, SIDNEY, M.D., Physician and Lecturer on Medicine at St. Mary's Hospital; Senior Physician to the London Fever Hospital, and to the Lock Hospital; 62, Upper Berkeley street, Portman square. *Trans.* 1.

1867 **Pick**, THOMAS PICKERING, Consulting Surgeon to St. George's Hospital; 18, Portman street, Portman square. C. 1884-5. V.P. 1893-4. *Referee*, 1882-3, 1891-93. *Sci. Com.* 1870, 1889—. *Lib. Com.* 1879-81.

1884 PITT, GEORGE NEWTON, M.D., Physician to, and Pathologist at, Guy's Hospital; 15, Portland place. *Referee*, 1897—. *Trans.* 1.

1889 PITTS, BERNARD, M.A., M.C., Surgeon to St. Thomas's Hospital and Lecturer on Surgery; Surgeon to the Hospital for Sick Children, Great Ormond street; 109, Harley street, Cavendish square. *Referee*, 1897—.

1899 PLAYFAIR, ERNEST, M.B., 57, Gloucester terrace, Hyde Park.

1901 PLIMMER, HARRY GEORGE, 28, St. John's Wood road.

1885 POLAND, JOHN, Surgeon to the City Orthopædic Hospital and Miller Hospital, Greenwich; 2, Mansfield street, Cavendish square.

1884 POLLARD, BILTON, B.S., Surgeon to University College Hospital; Consulting Surgeon to the North-Eastern Hospital for Children; 24, Harley street, Cavendish square. *Trans.* 1.

1865 **Pollock**, JAMES EDWARD, M.D., Consulting Physician to the Hospital for Consumption, Brompton; 52, Upper Brook street, Grosvenor square. C. 1882-3. V.P. 1896-7. *Referee*, 1872-81.

Elected

1894 POLLOCK, WILLIAM RIVERS, M.B., B.C., Assistant Obstetric Physician to the Westminster Hospital ; 56, Park street, Grosvenor square.

1871 POORE, GEORGE VIVIAN, M.D., Professor of Medical Jurisprudence and Clinical Medicine in University College, London; Physician to University College Hospital; 24A, Portland place. C. 1890-91. *Referee*, 1887-9, 1892—. *Lib. Com.* 1895—. *Trans.* 2.

1867 POWELL, SIR RICHARD DOUGLAS, Bart., M.D., K.C.V.O., Physician Extraordinary to H.M. the King; Physician to, and Lecturer on Medicine at, the Middlesex Hospital; Consulting Physician to the Hospital for Consumption, Brompton ; 62, Wimpole street, Cavendish square. S. (Oct.) 1883-5. C. 1887-8. *Referee*, 1879-83, 1886. *Trans.* 3.

1887 POWER, D'ARCY, M.A., M.B., Assistant Surgeon at St. Bartholomew's Hospital; Surgeon to the Victoria Hospital for Children, Chelsea; 10A, Chandos street, Cavendish Square. *Lib. Com.* 1896—. *Trans.* 2.

1867 **Power**, HENRY, Consulting Ophthalmic Surgeon to St. Bartholomew's Hospital; 37A, Great Cumberland place, Hyde Park. C. 1882-3. V.P. 1892-3. *Referee*, 1870-81, 1891-2. *Sci. Com.* 1870, 1889—. *Lib. Com.* 1872-8.

1883 PRINGLE, JOHN JAMES, M.B., C.M., Physician in Charge of Skin Department at the Middlesex Hospital; 23, Lower Seymour street, Portman square. *Trans.* 2.

1874 PURVES, WILLIAM LAIDLAW, Aural Surgeon to Guy's Hospital ; 20, Stratford place, Oxford street. *Trans.* 2.

1877 PYE-SMITH, PHILIP HENRY, M.D., F.R.S., Physician to and Lecturer on Medicine at, Guy's Hospital; 48, Brook street, Grosvenor square. C. 1893-4. *Lib. Com.* 1887-93, 1899—. *Referee*, 1897—. *Trans.* 1.

1898 RAMSAY, HERBERT MURRAY, 35A, Hertford street.

1893 RANKIN, GUTHRIE, 4, Chesham street, Belgrave square.

1899 RAWLING, LOUIS BATHE, M.B., B.C., St. Bartholomew's Hospital.

Elected

1892 RAYNER, HENRY, M.D., Lecturer on Psychological Medicine to St. Thomas's Hospital; 16, Queen Anne street, Cavendish square.

1869 READ, THOMAS LAURENCE, 11, Petersham terrace, Queen's gate. C. 1901—.

1891 REECE, RICHARD JAMES, 62, Addison gardens.

1891 RENDEL, ARTHUR BOWEN, M.A., M.B., B.C., 43, Albion street, Hyde Park.

1887 RICHARDSON, GILBERT, M.A., M.D., Hillside, Putney hill.

1863 RINGER, SYDNEY, M.D., F.R.S., Holme Professor of Clinical Medicine in University College, London, and Physician to University College Hospital; 15, Cavendish place, Cavendish square. C. 1881-2. V.P. 1900—. *Referee*, 1873-80, 1889-97. *Trans.* 6.

1900 RIVIERE, CLIVE, M.B., 82, Finchley road.

1896 ROBERTS, CHARLES HUBERT, M.D., Physician to Out-Patients, Samaritan Hospital for Women; Physician to Out-patients, Queen Charlotte's Lying-in Hospital, London; 21, Welbeck street.

1893 ROBERTS, D. WATKIN, M.D., 56, Manchester street, Manchester square.

1878 ROBERTS, FREDERICK THOMAS, M.D., Professor of Medicine, and of Clinical Medicine, in University College, London; Physician to University College Hospital; Consulting Physician to the Hospital for Consumption, Brompton; 102, Harley street, Cavendish square. C. 1894-5. *Referee*, 1899—. *Sci. Com.* 1889—.

1898 ROBERTSON, F. W., M.D., "Ravenstone," Lingfield road, Wimbledon, Surrey.

1901 ROBINSON, GEORGE HENKELL DRUMMOND, M.D., 84, Park street, Grosvenor square.

Elected

1896 Robinson, Henry Betham, M.S., Assistant Surgeon to, and Surgeon in Charge of the Throat Department, St. Thomas's Hospital; Assistant Surgeon to the East London Hospital for Children, Shadwell; 1, Upper Wimpole street.

1890 Rolleston, Humphry Davy, M.D., Physician to, and Lecturer on Pathology at, St. George's Hospital; Senior Physician to Out-patients, Victoria Hospital for Children; 55, Upper Brook street, Grosvenor square.

1857 **Rose**, Henry Cooper, M.D., 16, Warwick road, Maida Vale. C. 1886-7. *Trans.* 1.

1883 Rose, William, M.B., Professor of Clinical Surgery in King's College; Senior Surgeon to King's College Hospital; Consulting Surgeon to the Royal Free Hospital; 17, Harley street, Cavendish square. C. 1900—1901.

1888 Roughton, Edmund Wilkinson, B.S., M.D., Surgeon and Surgical Tutor to the Royal Free Hospital; 38, Queen Anne street. *Trans.* 1.

1882 Routh, Amand Jules McConnel, M.D., B.S., Obstetric Physician to, and Lecturer on Midwifery at, the Charing Cross Hospital; Physician to the Samaritan Free Hospital for Women and Children; 14A, Manchester square. *Lib. Com.* 1900—. *Referee*, 1900—.

1849 **Routh**, Charles Henry Felix, M.D., Consulting Physician to the Samaritan Free Hospital for Women and Children; 52, Montagu square. *Lib. Com.* 1854-5. *Trans.* 1.

1891 Russell, J. S. Risien, M.D., Assistant Physician to University College Hospital, and Pathologist to the National Hospital for the Paralysed and Epileptic, Queen square; 44, Wimpole street, Cavendish square. *Trans.* 1.

Elected

1900 RYALL, CHARLES, 51, Queen Anne street.

1886 SAINSBURY, HARRINGTON, M.D., Physician to the Royal Free Hospital; Physician to the City of London Hospital for Diseases of the Chest; 52, Wimpole street, Cavendish square. *Trans.* 1.

1899 SANDILANDS, JOHN EDWARD, M.B., 1, Montague square.

1869 **Sansom**, ARTHUR ERNEST, M.D., Physician to the London Hospital; Consulting Physician, North-Eastern Hospital for Children; 84, Harley street, Cavendish square. C. 1887-8. *Referee*, 1889—. *Trans.* 3.

1879 SAVAGE, GEORGE HENRY, M.D., Lecturer on Mental Diseases at Guy's Hospital; 3, Henrietta street, Cavendish square. C. 1898-9.

1892 SCHORSTEIN, GUSTAVE, M.A., M.B., B.Ch., D.P.H., Assistant Physician to the London Hospital, and to the Hospital for Consumption, Brompton; 11, Portland place.

1899 SCOTT, LINDLEY MARCROFT, M.D., 98, Sloane street.

1882 SCRIVEN, JOHN BARCLAY, Brigade Surgeon, Bengal (retired); 95, Oxford gardens, North Kensington.

1863 **Sedgwick**, WILLIAM, 101, Gloucester place, Portman square. C. 1884-5. *Trans.* 3.

1892 SEGUNDO, CHARLES SEMPILL DE, M.B., B.S., 6, Brook street, Hanover square.

1892 SELWYN-HARVEY, JOHN STEPHENSON, M.D., 1, Astwood road, Cromwell road.

1877 SEMON, SIR FELIX, M.D., Physician Extraordinary to H.M. the King; Physician for Diseases of the Throat to the National Hospital for Epilepsy and Paralysis, Queen square; 39, Wimpole street, Cavendish square. C. 1895-7. *Lib. Com.* 1894-5. *Trans.* 3.

Elected

1900 SEQUEIRA, JAMES HARRY, M.D., 13, Welbeck street.

1894 SEWILL, JOSEPH SEFTON, 9A, Cavendish square.

1882 SHARKEY, SEYMOUR JOHN, M.D., Physician to, and Joint Lecturer on Medicine at, St. Thomas's Hospital; 22, Harley street, Cavendish square. C. 1899-1900. *Referee*, 1897-9. *Trans.* 2.

1900 SHAW, HAROLD BATTY, M.D., 7, Devonshire street, Portland place.

1886 SHAW, LAURISTON ELGIE, M.D., Physician to Guy's Hospital; 64, Harley street, Cavendish square.

1884 SHEILD, ARTHUR MARMADUKE, M.B., B.C., Assistant Surgeon to St. George's Hospital; 4, Cavendish place. *Referee*, 1897—. *Trans.* 6.

1896 SHORE, THOMAS WILLIAM, M.D., Heathfield, Alleyn park, Dulwich.

1893 SIBLEY, WALTER KNOWSLEY, M.D., B.C., Senior Physician to Out-patients, North-West London Hospital; 1, Duke street mansions, Grosvenor square.

1848 **Sieveking**, SIR EDWARD HENRY, M.D., LL.D., F.S.A., Physician Extraordinary to H.M. the King; Consulting Physician to St. Mary's and the Lock Hospitals; 17, Manchester square. C. 1859-60. S. 1861-3. V.P. 1873-4. L. 1881-2. P. 1888-9. *Referee*, 1855-8, 1864-72, 1875-80. *Sci. Com.* 1862. *Trans.* 2.

1886 SILCOCK, ARTHUR QUARRY, B.S., Surgeon in charge of Out-patients, and Teacher of Operative Surgery, St. Mary's Hospital; Surgeon to the Royal London Ophthalmic Hospital; 52, Harley street, Cavendish square. *Lib. Com.* 1895—.

1842 **Simon**, SIR JOHN, K.C.B., F.R.S., Hon. M.D.Dublin, 1887, Consulting Surgeon to St. Thomas's Hospital; 40, Kensington square. C. 1854-5. V.P. 1865. *Referee*, 1851-3, 1866-81. *Trans.* 1.

Elected

1899 SIMPSON, WILLIAM JOHN RITCHIE, M.D., 12, Gloucester place, Portman square.

1892 SIMS, FRANCIS MANLEY BOLDERO, 12, Hertford street, Mayfair.

1894 SLATER, CHARLES, M.B., 81, St. Ermin's mansions, Westminster.

1890 SMALE, MORTON, Surgeon Dentist to St. Mary's Hospital; 22A, Cavendish square.

1879 SMITH, E. NOBLE, Surgeon to the City Orthopædic Hospital; Surgeon to All Saints' Children's Hospital; Orthopædic Surgeon to the British Home for Incurables; 24, Queen Anne street, Cavendish square.

1881 SMITH, EUSTACE, M.D., Physician to H.M. the King of the Belgians; Physician to the East London Children's Hospital, and to the Victoria Park Hospital for Diseases of the Chest; 15, Queen Anne street, Cavendish square. C. 1899-1900.

1866 SMITH, HEYWOOD, M.A., M.D., 18, Harley street, Cavendish square.

1889 SMITH, ROBERT PERCY, M.D., B.S., Lecturer on Psychological Medicine, Charing Cross Hospital; 36, Queen Anne street.

1892 SMITH, SOLOMON CHARLES, M.D., Four Oaks, Walton-on-Thames, Consulting Surgeon to the Royal Halifax Infirmary.

1863 **Smith**, SIR THOMAS, Bart., Honorary Sergeant-Surgeon to H.M. the King; Consulting Surgeon to St. Bartholomew's Hospital; 5, Stratford place, Oxford street. S. 1870-2. C. 1875-6. V.P. 1887-8. *Referee*, 1873-4, 1880-6. *Sci. Com.* 1867. *Trans.* 4.

Elected

1872 SMITH, THOMAS GILBART, M.D., Physician to the London Hospital; Physician to the Royal Hospital for Diseases of the Chest, City road; 68, Harley street, Cavendish square. C. 1890. *Trans.* 1.

1873 SMITH, W. JOHNSON, Surgeon to the Seamen's Hospital Society, Greenwich.

1874 *Smith*, WILLIAM ROBERT, M.D., D.Sc., F.R.S.Edin., Barrister-at-Law, Professor of Forensic Medicine, and Director of the Laboratories of State Medicine in King's College, London; Medical Officer to the School Board for London; 74, Great Russell street. *Trans.* 1.

1889 SPENCER, HERBERT R., M.D., B.S., Professor of Midwifery in University College; Obstetric Physician to University College Hospital; 104, Harley street. *Referee*, 1894—.

1887 SPENCER, WALTER GEORGE, M.B., M.S., Surgeon to, and Lecturer on Physiology at, the Westminster Hospital; 35, Brook street, Grosvenor square. *Trans.* 2.

1888 SPICER, ROBERT HENRY SCANES, M.D., Surgeon to the Department for Diseases of the Throat, St. Mary's Hospital; 28, Welbeck street, Cavendish square.

1890 SPICER, WILLIAM THOMAS HOLMES, M.B., 5, Wimpole street, Cavendish square.

1875 SPITTA, EDMUND JOHNSON, Ivy House, 31, South Side, Clapham Common, Surrey.

1885 SQUIRE, JOHN EDWARD, M.D., Physician to the North London Hospital for Consumption; 2, Harley street, Cavendish square. *Trans.* 2.

1897 STAINER, EDWARD, M.A., M.B., 60, Wimpole street.

1899 STEWART, PURVES, M.D., 7, Harley street.

1856 **Stocker**, ALONZO HENRY, M.D., Peckham House, Peckham.

1884 STONHAM, CHARLES, Surgeon to, and Lecturer on Surgery and Teacher of Operative Surgery at, the Westminster Hospital; Surgeon to the Poplar Hospital for Accidents; 4, Harley street, Cavendish square.

Elected

1896 SUTHERLAND, GEORGE ALEXANDER, M.D., Physician to Paddington Green Children's Hospital; Assistant Physician to the North-West London Hospital; 73, Wimpole street, Cavendish square.

1896 SWAN, CHARLES ROBERT JOHN ATKIN, M.B., B.Ch., 4, Devonport street, Hyde Park.

1890 SYERS, HENRY WALTER, M.D., 75, Wimpole street.

1886 SYMONDS, CHARTERS JAMES, M.S., M.D., Surgeon to, and Surgeon in charge of the Throat Department at, Guy's Hospital; 58, Portland place.

1875 TAY, WABEN, Senior Surgeon to the London Hospital, to the Royal London Ophthalmic Hospital, and to the Hospital for Diseases of the Skin, Blackfriars; Consulting Surgeon to the North-Eastern Hospital for Children; 4, Finsbury square.

1873 TAYLOR, FREDERICK, M.D., *Trustee;* Physician to, and Lecturer on Medicine at, Guy's Hospital; Consulting Physician to the Evelina Hospital for Sick Children; 20, Wimpole street, Cavendish square. S. 1889-93. C. 1894-6. *Sci. Com.* 1889—. *Referee,* 1887-8, 1899—. *Trans.* 3.

1893 TAYLOR, JAMES, M.D., Assistant Physician to the National Hospital for the Paralysed and Epileptic; Physician to the North-Eastern Hospital for Children, and to the National Orthopædic Hospital; 49, Welbeck street, Cavendish square. *Trans.* 1.

1890 TAYLOR, SEYMOUR, M.D., Assistant Physician, West London Hospital; 16, Seymour street, Portman square.

1859 TEGART, EDWARD, 60, Scarsdale Villas, Kensington. C. 1888-9.

1874 THIN, GEORGE, M.D., 63, Harley street, Cavendish square. C. 1893-4. *Trans.* 14.

1900 THOMPSON, CHARLES HERBERT, M.D., 17, New Cavendish street, Portland place.

Elected

1862 **Thompson**, EDMUND SYMES, M.D., Consulting Physician to the Hospital for Consumption, Brompton; Gresham Professor of Medicine; 33, Cavendish square. S. 1871-4. C. 1878-9. *Sci. Com.* 1889—. *Referee*, 1876-7. *Trans.* 1.

1852 **Thompson**, SIR HENRY, Bart., Surgeon-Extraordinary to H.M. the King of the Belgians; Emeritus Professor of Clinical Surgery in University College, London; and Consulting Surgeon to University College Hospital; 35, Wimpole street, Cavendish square. V.P. 1888. C. 1869. *Trans.* 8.

1862 **Thompson**, REGINALD EDWARD, M.D., Consulting Physician to the Hospital for Consumption, Brompton; 73, Lillie road, West Kensington. C. 1879. S. 1880-82. V.P. 1883-4. *Referee*, 1873-8. *Sci. Com.* 1867. *Trans.* 2.

1899 THOMSON, HERBERT CAMPBELL, M.D., 34, Queen Anne street. *Trans.* 1.

1892 THOMSON, STCLAIR, M.D., Physician to the Throat Hospital, Golden Square; Surgeon to the Royal Ear Hospital, London; 28, Queen Anne street, Cavendish square. *Trans.* 1.

1900 THOMSON-WALKER, JOHN WILLIAM, M.B., 8, Cavendish place.

1892 THORNE, WILLIAM BEZLY, M.D., 53, Upper Brook street.

1899 THURSFIELD, JAMES HUGH, M.D., 10, Bentinck street, Manchester square. *Trans.* 1.

1889 TIRARD, NESTOR ISIDORE CHARLES, M.D., Professor of Materia Medica and Therapeutics, King's College; Physician to King's College Hospital, and Physician to the Evelina Hospital for Sick Children; 74, Harley street, Cavendish square.

1872 TOMES, CHARLES SISSMORE, M.A., F.R.S., 9, Park crescent, Portland place. C. 1887. V.P. 1897-99. *Lib. Com.* 1879.

Elected

1882 TOOTH, HOWARD HENRY, M.D., Physician to the National Hospital for the Paralysed and Epileptic, Queen square; Assistant Physician to St. Bartholomew's Hospital; 34, Harley street, Cavendish square. *Sci. Com.* 1896—.

1879 TREVES, SIR FREDERICK, C.B., K.C.V.O., Honorary Sergeant-Surgeon to H.M. the King; Surgeon-in-Ordinary to H.R.H. the Prince of Wales; Consulting Surgeon to the London Hospital; 6, Wimpole street, Cavendish square. C. 1895-6. *Referee*, 1890-95. *Sci. Com.* 1889-95. *Trans.* 6.

1859 **Truman**, EDWIN THOMAS, Surgeon-Dentist to His Majesty's Household; 23, Old Burlington street.

1897 TUNNICLIFFE, FRANCIS WHITTAKER, M.D., 6, Devonshire street, Portland place.

1889 TURNBULL, GEORGE LINDSAY, M.D., Grove House, 76, Ladbroke grove.

1882 TURNER, GEORGE ROBERTSON, Surgeon to, and Joint Lecturer on Surgery at, St. George's Hospital; Visiting Surgeon to the Seamen's Hospital, Greenwich; 41, Half Moon street, Piccadilly. *Trans.* 1.

1898 TURNER, WILLIAM, M.B., B.S., Assistant Surgeon, Westminster Hospital; 53, Queen Anne street, Cavendish square.

1896 TURNER, WILLIAM ALDREN, M.D., Assistant Physician to King's College Hospital and to the National Hospital for the Paralysed and Epileptic, Queen Square; 13, Queen Anne street, Cavendish square.

1896 TURNEY, HORACE GEORGE, M.D., Joint Lecturer on Pathology and Assistant Physician to St. Thomas's Hospital; 68, Portland place. *Trans.* 1.

1892 TWEEDY, JOHN, Professor of Ophthalmic Medicine and Surgery in University College, Ophthalmic Surgeon to University College Hospital, and Surgeon to the Royal London Ophthalmic Hospital; 100, Harley street, Cavendish square.

1876 VENN, ALBERT JOHN, M.D., 63, Grosvenor street.

Elected

1870 VENNING, EDGCOMBE, 30, Cadogan place. C. 1898-1900.

1891 VOELCKER, ARTHUR FRANCIS, M.D., B.S., Assistant Physician to, and Lecturer on Pathology at, the Middlesex Hospital; Assistant Physician, Hospital for Sick Children, Great Ormond street; 31, Harley street.

1896 WAGGETT, ERNEST, M.B., B.C., Assistant Surgeon, London Throat Hospital; 45, Upper Brook street.

1884 WAKLEY, THOMAS, jun., 5, Queen's Gate, South Kensington.

1896 WALDO, FREDERICK JOSEPH, M.D., City Coroner, 1, Plowden buildings, Temple.

1900 WALKER, H. ROE, 20, St. James's place, St. James's street.

1887 WALLACE, EDWARD JAMES, M.D., 22, Hans crescent, Chelsea.

1883 WALLER, AUGUSTUS, M.D., F.R.S., Lecturer on Physiology, St. Mary's Hospital; Weston Lodge, 16, Grove End road, St. John's Wood. *Referee*, 1895—.

1888 WALLIS, FREDERICK CHARLES, M.B., B.C., Assistant Surgeon to the Charing Cross Hospital; 107, Harley street, Cavendish square.

1896 WALSHAM, HUGH, M.A., M.D., Assistant Physician to the City of London Hospital for Diseases of the Chest; Assistant Medical Officer in Electrical Department, St. Bartholomew's Hospital; 114, Harley street, Cavendish square.

1873 **Walsham**, WILLIAM JOHNSON, C.M., Surgeon to, and Lecturer on Surgery at, St. Bartholomew's Hospital; Consulting Surgeon to the Metropolitan Hospital; 77, Harley Street, Cavendish square. C. 1888-9. *Referee*, 1895—. *Lib. Com.* 1882-5. *Trans.* 8.

1899 WALTERS, FREDERICK RUFENACHT, M.D., 21, Wimpole street, Cavendish square.

1886 WARD, ALLAN OGIER, M.D., 73, Cheapside.

1890 WARD, ARTHUR HENRY, Surgeon to Out-patients, Lock Hospital; 31, Grosvenor street.

1894 WARD-HUMPHREYS, GEORGE HERBERT, 7, Cavendish place, Cavendish square.

Elected

1891 WARING, H. J., M.B., M.S., B.Sc., Surgical Registrar and Demonstrator of Operative Surgery, St. Bartholomew's Hospital; Surgeon, Metropolitan Hospital; 37, Wimpole street.

1877 WARNER, FRANCIS, M.D., Physician to, and Lecturer on Materia Medica and Therapeutics at, the London Hospital; 5, Prince of Wales terrace, Kensington Palace. C. 1899—1901. *Trans.* 3.

1889 WASHBOURN, JOHN WICHENFORD, M.D., Physician to, Joint Lecturer on Physiology, and Lecturer on Bacteriology at, Guy's Hospital; Physician to the London Fever Hospital; 6, Cavendish place. *Trans.* 1.

1894 WATERHOUSE, HERBERT FURNIVALL, C.M., Senior Assistant Surgeon and Lecturer on Anatomy, Charing Cross Hospital; Surgeon, Victoria Hospital for Children; 81, Wimpole street.

1861 **Watson**, WILLIAM SPENCER, M.B., 61, Bedford gardens, Campden hill, Kensington. C. 1883-4. *Trans.* 1.

1892 WEAVER, FREDERICK POYNTON, M.D., Cedar Lawn, Hampstead heath.

1891 **Weber**, FREDERIC PARKES, M.D., Physician to the German Hospital, Dalston; 19, Harley street. *Trans.* 1. *Pro.* 1.

1857 WEBER, SIR HERMANN, M.D., Consulting Physician to the German Hospital; 10, Grosvenor street, Grosvenor square. C. 1874-5. V.P. 1885-6. *Sci. Com.* 1889—. *Referee*, 1869-73, 1878-84. *Lib. Com.* 1864-73. *Trans.* 6.

1895 WELLS, SYDNEY RUSSELL, M.D., 24, Somerset street, Portman square.

1877 WEST, SAMUEL, M.D., Assistant Physician to St. Bartholomew's Hospital; Senior Physician to the Royal Free Hospital; 15, Wimpole street, Cavendish square. C. 1894-5. *Lib. Com.* 1892-4. *Trans.* 7.

Elected

1888 WETHERED, FRANK JOSEPH, M.D., Assistant Physician to the Hospital for Consumption, Brompton; 83, Harley street, Cavendish square. *Trans.* 1.

1881 WHARRY, ROBERT, M.D., 7, Cambridge gate, Regent's park.

1875 WHIPHAM, THOMAS TILLYER, M.D., Consulting Physician to St. George's Hospital; 11, Grosvenor street, Grosvenor square. C. 1892-3.

1891 WHITE, CHARLES PERCIVAL, M.B., B.C., 22, Cadogan gardens.

1881 WHITE, WILLIAM HALE, M.D., Physician to, and Lecturer on Materia Medica at, Guy's Hospital; 65, Harley street, Cavendish square. C. 1900—. *Referee*, 1888-97, 1899-1900. *Trans.* 4.

1890 WHITE-COOPER, W. G. O., M.B., 5, Courtfield road, Gloucester road.

1897 WHITFIELD, ARTHUR, M.D., 12, Upper Berkeley street.

1899 WHITING, ARTHUR J., M.D., 142, Harley street.

1877 WHITMORE, WILLIAM TICKLE, Consulting Surgeon to the Gordon Hospital for Diseases of the Rectum; 7, Arlington street, Piccadilly.

1863 **Wilks**, SIR SAMUEL, Bart., M.D., LL.D., F.R.S., Physician Extraordinary to Her late Majesty Queen Victoria, Physician in Ordinary to their Royal Highnesses the Duke and Duchess of Connaught; Consulting Physician to Guy's Hospital; 8, Prince Arthur road, Hampstead. *Referee*, 1872-81.

1890 WILLCOCKS, FREDERICK, M.D., Physician to Out-Patients, and Lecturer on Materia Medica and Therapeutics, at the Charing Cross Hospital; Physician to the Evelina Hospital for Sick Children; 14, Mandeville place, Manchester square.

Elected

1865 **Willett**, ALFRED, *Trustee;* Surgeon to St. Bartholomew's Hospital; Surgeon to St. Luke's Hospital; 36, Wimpole street, Cavendish square. C. 1880-81. V.P. 1890-91. *Referee*, 1882-89, 1892—. *Bldg. Com.* 1889-92. *Ho. Com.* 1892-8. *Trans.* 2.

1887 WILLETT, EDGAR, M.B., 25, Welbeck street, Cavendish square.

1888 WILLIAMS, CAMPBELL, 18, Queen Anne street.

1866 **Williams**, CHARLES THEODORE, M.A., M.D., *Trustee for Debenture-holders;* Consulting Physician to the Hospital for Consumption and Diseases of the Chest, Brompton; 2, Upper Brook street, Grosvenor square. C. 1884-5. V.-P. 1900—. *Referee*, 1888-1900. *Lib. Com.* 1880-3. *Ho. Com.* 1900. *Sci. Com.* 1889—. *Trans.* 6.

1881 WILLIAMS, DAWSON, M.D., Physician to the East London Hospital for Children; 2, Wyndham place, Bryanston square. *Trans.* 1.

1900 WILLIAMS, HUGH LLOYD, 2, Upper Wimpole street.

1872 WILLIAMS, SIR JOHN, Bart., M.D., Physician-Accoucheur to H.R.H. the Princess of Wales, Physician to H.R.H. the Princess Beatrice; Emeritus Professor of Obstetric Medicine, University College, London; Consulting Obstetric Physician to University College Hospital; 63, Brook street, Grosvenor square. C. 1891. *Referee*, 1878-90. *Lib. Com.* 1876-82.

1890 WILLS, WILLIAM ALFRED, M.D., Assistant Physician to the Westminster Hospital; Senior Physician to the North-Eastern Hospital for Children; 29, Lower Seymour street, Portman square.

1879 WOAKES, EDWARD, M.D., Senior Aural Surgeon to the London Hospital; 78, Harley street, Cavendish square.

1887 WOOD, THOMAS OUTTERSON, M.D., Senior Physician to the West End Hospital for Nervous Diseases; 40, Margaret street, Cavendish square.

Elected

1891 WOODFORDE, ALFRED POWNALL, 160, Goldhawk road, Shepherd's Bush.

1890 WYNTER, WALTER ESSEX, M.D., Assistant Physician to the Middlesex Hospital; 30, Upper Berkeley street, Portman square.

LIST OF RESIDENT FELLOWS

ARRANGED ACCORDING TO

DATE OF ELECTION

1842 Sir John Simon, K.C.B., F.R.S.
1845 Edward U. Berry.
1848 Sir Edward H Sieveking, M.D.
John Clarke, M.D.
1849 C. H. F. Routh, M.D.
1851 John Birkett.
John A. Kingdon.
1852 Sir Henry Thompson, Bart.
1853 Robert Brudenell Carter.
1854 Sir Alfred B. Garrod, M.D., F.R.S.
1856 William Bird.
Jonathan Hutchinson, F.R.S.
Timothy Holmes.
Alonzo H. Stocker, M.D.
1857 Sir Hermann Weber, M.D.
Henry Cooper Rose, M.D.
Henry Walter Kiallmark.
1858 John William Ogle, M.D.
1859 Wm. Howship Dickinson, M.D.
Edwin Thomas Truman.
Richard Barwell.
Edward Tegart.
1860 William Ogle, M.D.
Thomas Bryant.
John Couper.
Henry Howard Hayward.
1861 William Spencer Watson.
1862 Lionel Smith Beale, M.B., F.R.S.
Edmund Symes Thompson, M.D.
1862 Reginald Edward Thompson, M.D.
George Cowell.
1863 Sir Samuel Wilks, Bt., M.D., F.R.S.
Samuel Fenwick, M.D.
Sydney Ringer, M.D., F.R.S.
Sir Thomas Smith, Bart.
Arthur B. R. Myers.
William Sedgwick.
1864 Thomas William Nunn.
1865 James Edward Pollock, M.D.
George Fielding Blandford, M.D.
Sir Dyce Duckworth, M.D.
Frederick W. Pavy, M.D., F.R.S.
John Langton.
Frederick James Gant.
Alfred Willett.
Alfred Cooper.
Christopher Heath.
1866 Samuel Jones Gee, M.D.
Charles Theodore Williams, M.D.
Heywood Smith, M.D.
Sir William Selby Church, Bart., M.D.
1867 Sir R. Douglas Powell, Bart., M.D.
F. Howard Marsh.
Henry Power.
Thomas Pickering Pick.
1868 H. Charlton Bastian, M.D., F.R.S.
Sir W. H. Broadbent, Bart., M.D.

1868 Thomas Buzzard, M.D.
Walter Butler Cheadle, M.D.
T. Henry Green, M.D.
George Eastes.
1869 Joseph Frank Payne, M.D.
Arthur E. Sansom, M.D.
Thomas Laurence Read.
1870 J. Warrington Haward.
Edgcombe Venning.
Clement Godson, M.D.
Reginald Harrison.
Robert Leamon Bowles, M.D.
1871 William Cayley, M.D.
Sir T. Lauder Brunton, M.D., F.R.S.
J. Hughlings Jackson, M.D., F.R.S.
George Vivian Poore, M.D.
Philip Frank, M.D.
1872 T. Gilbart-Smith, M.D.
George B. Brodie, M.D.
Sir John Williams, Bart., M.D.
Sir J. Fayrer, M.D., F.R.S.
Charles S. Tomes, M.A., F.R.S.
Sir William Bartlett Dalby.
1873 William Miller Ord, M.D.
Frederick Taylor, M.D.
Norman Moore, M.D.
John Curnow, M.D.
Sir William R. Gowers, M.D., F.R.S.
Sir Wm. Guyer Hunter, M.D.
Jeremiah McCarthy.
Wm. Johnson Smith.
Alex. O. MacKellar.
Henry T. Butlin.
Charles Higgens.
William J. Walsham.
1874 Alfred Lewis Galabin, M.D.
George Thin, M.D.
John Mitchell Bruce, M.D.
Henry Morris.
William Laidlaw Purves.
William Harrison Cripps.
Henry G. Howse..M.S.
Herbert William Page.
Frederic Durham.
William Robert Smith, M.D.
1875 Thomas T. Whipham, M.D.
Thomas Crawford Hayes, M.D.
Waren Tay.
Edmund J. Spitta.
Samuel C. Osborn.
Fletcher Beach, M.B.
1876 Sir Thomas Barlow, Bart., K.C.V.O., M.D.
Wm. Lewis Dudley, M.D.
Albert J. Venn, M.D.
N. Charles Macnamara.
1877 Sir Felix Semon, M.D.
Sidney Coupland, M.D.
Francis Warner, M.D.
William Ewart, M.D.
Alfred Pearce Gould, M.S.
Rickman J. Godlee, M.S.
Alban H. G. Doran.
George Ernest Herman, M.B.
Samuel West, M.D.
John Abercrombie, M.D.
George Allan Heron, M.D.
Joseph A. Ormerod, M.D.
P. Henry Pye-Smith, M.D., F.R.S.
Sir William Henry Bennett.
William T. Whitmore.
1878 Sir Jas. Crichton-Browne, M.D.
Fred. T. Roberts, M.D.
Lord Lister, F.R.S.
Clinton T. Dent.
John H. Morgan, C.V.O.
Donald W. Charles Hood, M.D.
1879 Edward Woakes, M.D.
Malcolm A. Morris.
A. E. Cumberbatch.
Edmund Owen.
Arthur E. J. Barker.
Sir Fredk. Treves, C.B., K.C.V.O.
Thomas John Maclagan, M.D.
Andrew Clark.
Francis Henry Champneys, M.D.
William Watson Cheyne, F.R.S.
George Henry Savage, M.D.
H. H. Clutton, M.A.
Frederic S. Eve.
E. Noble Smith.
William Henry Allchin, M.D.
1880 Robert Alex. Gibbons, M.D.
David Ferrier, M.D., F.R.S.
Vincent Dormer Harris, M.D.
Edmund Distin Maddick.
Jas. John MacWhirter Dunbar, M.D.
James William Browne, M.B.
William Appleton Meredith, M.B.
Malcolm Macdonald McHardy.
A. Boyce Barrow.
William Murrell, M.D.
George Ogilvie, M.B.
Charles Edward Beevor, M.D.
Thomas Colcott Fox, M.B
George Henry Makins, C.B.
1881 Francis de Havilland Hall, M.D.

1881 Robert Wharry, M.D.
Richard Clement Lucas, B.S.
Stephen Mackenzie, M.D.
William Hale White, M.D.
Eustace Smith, M.D.
Percy Kidd, M.D.
Oswald A. Browne, M.D.
W. Bruce Clarke, M.B.
Dawson Williams, M.D.
George Lindsay Johnson, M.D.
Henry Edward Juler.
Jonathan F. C. H. Macready.
C. B. Lockwood.

1882 Philip J. Hensley, M.D.
Ernest Clarke, M.D., B.S.
John Barclay Scriven.
George Robertson Turner.
Howard Henry Tooth, M.D.
Herbert Isambard Owen, M.D.
Charles R. B. Keetley.
Anthony A. Bowlby, C.M.G.
Amand J. McC. Routh, M.D.
Seymour J. Sharkey, M.D.
William Lang.
Henry Radcliffe Crocker, M.D.

1883 Edwin Clifford Beale, M.A., M.B.
James Kingston Fowler, M.D.
James Frederic Goodhart, M.D.
John Charles Galton, M.A.
W. Hamilton A. Jacobson, M.Ch.
Walter H. Jessop, M.B.
Walter Edmunds, M.C.
Victor A. Horsley, F.R.S.
Dudley Wilmot Buxton, M.D.
Charles Douglas F. Phillips, M.D.
John James Pringle, M.B.
Henry Roxburgh Fuller, M.D.
Wilmot Parker Herringham, M.D.
Augustus Waller, M.D.
William Pasteur, M.D.
John Bland-Sutton.
William Rose, M.B.
Robert Marcus Gunn, M.B.

1884 George Newton Pitt, M.D.
Charles Stonham.
Stanley Boyd, M.B.
William Arbuthnot Lane, M.S.
Arthur Marmaduke Sheild, M.B.
Sidney Harris Cox Martin, M.D., F.R.S.
George Lawson.
Thomas Wakley, jun.
F. Swinford Edwards.
James Johnston, M.D.

1884 William Duncan, M.D.
Charles Chinner Fuller.
George Richard Turner Phillips.
Bilton Pollard.

1885 Alexander Haig, M.D.
Theodore Dyke Acland, M.D.
Frederick Walker Mott, M.D.
James Berry.
John Cahill, M.D.
John Poland.
A. C. Butler-Smythe.
Charles Alfred Ballance, M.S.
Walter S. A. Griffith, M.D.
John Edward Squire, M.D.
John D. Malcolm, M.B., C.M.
Phineas S. Abraham, M.D.
Henry Willingham Gell, M.B.

1886 Robert Maguire, M.D.
Harrington Sainsbury, M.D.
Cuthbert Hilton Golding-Bird, M.B.
Lauriston Elgie Shaw, M.D.
Charters James Symonds, M.S.
Robert Boxall, M.D.
Allan Ogier Ward, M.D.
Archibald Edward Garrod, M.D.
Stephen Paget.
William Radford Dakin, M.D.
Samuel Herbert Habershon, M.D.
Arthur Quarry Silcock.
Arthur H. N. Lewers, M.D.

1887 Walter George Spencer.
Thomas Outterson Wood, M.D.
Edgar William Willett, M.B.
Henry Lewis Jones, M.D.
Francis George Penrose, M.D.
Hugh Percy Dunn.
Frederic William Hewitt, M.D.
James Barry Ball, M.D.
Gilbert Richardson, M.D.
D'Arcy Power, M.B.
John Gay.
James Calvert, M.D.
Percy J. F. Lush, M.B.
Edward James Wallace, M.D.

1888 Robert Henry Scanes Spicer, M.D.
Jonathan Hutchinson, jun.
Campbell Williams.
James Donelan, M.B., C.M.
John Anderson, M.D., C.I.E.
Laurie Asher Lawrence.
Arthur Pearson Luff, M.D., B.Sc.
Albert Carless, M.S.
Frederick C. Wallis, M.B., B.C.
Charles James Cullingworth, M.D.

1888 Edmund Cautley, M.D., B.C.
H. Montague Murray, M.D.
Frank Joseph Wethered, M.D.
Edmund Wilkinson Roughton, B.S.
Frederick William Cock, M.D.
John Phillips, M.D.
Robert Henry Clarke, M.B.

1889 Montagu Handfield-Jones, M.D.
David Henry Goodsall.
Raymond Johnson, M.B.
John Fletcher Little, M.B.
Henry Work Dodd.
George Lindsay Turnbull, M.D.
Sidney Phillips, M.D.
William Charles Bull, M.B.
George P. Field.
John Wichenford Washbourn, M.D.
Charles Henry Cosens.
Henry Percy Dean, M.B., M.S.
Alfred Samuel Gubb, M.D.
William Hunter, M.D.
J. Inglis Parsons, M.D.
Bernard Pitts, M.B., M.C.
Robert Percy Smith, M.D., B.S.
Herbert R. Spencer, M.D., B.S.
Nestor Isidore Chas. Tirard, M.D.

1890 John Rose Bradford, M.D., F.R.S.
Roland Danvers Brinton, M.D.
Charles D. B. Hale, M.D.
Edwin Cooper Perry, M.D.
Morton Smale.
Frederick Willcocks, M.D.
William T. Holmes Spicer, M.B.
Thomas Henry Crowle.
Henry Walter Syers, M.D.
Seymour Taylor, M.D.
William Alfred Wills, M.D.
G. O. White-Cooper, M.B.
Herbert William Allingham.
William A. F. Bateman.
James Jackson Clarke, M.B.
Leonard G. Guthrie, M.D., B.Ch.
G. William Hill, M.D., B.Sc.
Edward Law, M.D., C.M.
Patrick Manson, M.D., C.M.
Humphry D. Rolleston, M.D.
Arthur Henry Ward.
Walter Essex Wynter, M.D., B.S.
Edward Lawrie, M.B.

1891 William Lee Dickinson, M.D.
Herbert P. Hawkins, M.D., B.Ch.
Cyril Ogle, M.A., M.B.
Arthur F. Voelcker, M.D., B.S.
Alfred Pownall Woodforde.

1891 Herbert T. Herring, M.B., B.S.
Ernest Muirhead Little.
Henry Charrington Martin, M.D.
Frederick William Andrewes, M.D.
Alfred Eddowes, M.D.
Herbert Morley Fletcher, M.D.
William Heaton Hamer, M.D.
William Bromfield Paterson.
Holburt Jacob Waring.
Frederic Parkes Weber, M.D.
F. E. Batten, M.D.
Thomas Jessopp Bokenham.
Norman Dalton, M.D.
P. R. W. De Santi.
P. W. Dove.
William J. Gow, M.D.
Charles Arthur Mercier, M.B.
Paul Frank Moline, M.B.
Edward Percy Paton, M.D.
Arthur Bowen Rendel, M.B., B.C.
James Samuel Risien Russell, M.D.
Charles Percival White, M.B., B.C.
W. Page May, M.D.
Richard J. Reece.

1892 J. Dundas Grant, M.D.
R. J. Bliss Howard, M.D.
Thomas Horrocks Openshaw, M.B.
William Bezly Thorne, M.D.
W. H. Russell Forsbrook, M.D.
John Harold.
John Alfred Masters, M.D.
Gustave Schorstein, M.B.
Charles Sempill de Segundo, M.B.
John Tweedy.
E. H. Myddelton-Gavey.
E. Matthews James.
J. S. Selwyn-Harvey, M.D.
StClair Thomson, M.D.
F. Manley B. Sims.
F. Poynton Weaver, M.D.
Henry Rayner, M.D.
H. Marmaduke Page.

1893 James Taylor, M.D.
Howard Barrett.
Robert Cozens Bailey, M.B.
Henry Albert Caley, M.D.
Arthur Edward Giles, M.D.
Miles Miley, M.B.
D. Watkin Roberts, M.D.
Leonard A. Bidwell.
Frédéric F. Burghard, M.D., M.S.
J. H. Drysdale, M.B.
William McAdam Eccles, M.S.

1893 Vaughan Harley, M.D.
George Herschell, M.D.
Arnold Lawson.
Guthrie Rankin.
Walter Knowsley Sibley, M.D.
1894 Richard Gill.
Joseph Sefton Sewill.
Thomas Vincent Dickinson, M.D.
Herbert Edward Durham, M.B.
Alexander Morison, M.D.
L. Hemington Pegler, M.D.
Herbt. Furnivall Waterhouse, C.M.
Percy Furnivall.
R. L. Langdon-Down, M.B., B.C.
Allan Macfadyen, M.D., B.S.
Ernst Michels, M.D.
Wm. Rivers Pollock, M.B., B.C.
Charles Slater, M.B.
1895 Charles Arthur Parker.
Sydney Russell Wells, M.D.
Alfred Milne Gossage, M.B.
Robert Murray Leslie, M.B.
James Galloway, M.D.
David Bridge Lees, M.D.
Arthur G. Phear, M.D.
1896 Joseph Lockhart Downes, M.B.
Edward Wilberforce Goodall, M.D.
James Ernest Lane.
George Alex. Sutherland, M.D.
Charles Buttar, M.D.
P. J. Freyer, M.D., I.M.S., M.A.
Percival Horton-Smith, M.D.
Thomas William Shore, M.D.
William Aldren Turner, M.D.
John Brian Christopherson, M.D.
Charles Hubert Roberts, M.D.
Charles R. J. Atkin Swan, M.B.
James Kingston Barton.
J. Walter Carr, M.D.
John H. Dauber, M.A., M.B., B.Ch.
Alexander Grant Russell Foulerton.
L. Vernon Jones, B.A., M.D., B.Ch.
Alexander MacGregor, M.D.
Henry Betham Robinson, M.S.
Horace George Turney, M.D.
Ernest Waggett, M.B., B.C.
Frederick Joseph Waldo, M.D.
Hugh Walsham, M.D.
1897 Comyns Berkeley, M.B., B.C.
William Arthur Brailey, M.D.
James Cantlie, M.B.
Raymond H. Payne Crawfurd, M.D.
Louis Jenner, M.B.
Francis Whittaker Tunnicliffe, M.D.
1897 Arthur Whitfield, M.D.
Edward Stainer, M.A., M.B.
Alfred G. Levy, M.D.
A. P. Beddard, M.B.
G. F. Blacker, M.D.
W. S. Colman, M.D.
F. W. Goodbody, M.D.
R. Hutchison, M.D.
Harold Low.
Christopher Addison, M.D.
1898 J. H. Bryant, M.D.
W. H. Corfield, M.D.
L. A. Dunn, M.S.
E. Hurry Fenwick.
A. Downing Fripp, M.S.
A. Corrie Keep, M.D.
A. C. Latham, M.D.
J. B. Lawford.
John McFadyean.
H. Murray Ramsay.
J. F. H. Broadbent, M.D.
H. Ronald Carter.
A. Stark Currie, M.D.
P. J. Edmunds, M.B.
Alexander Granville.
James Morrison, M.D.
J. S. Edkins.
Thomas J. Horder, M.D.
F. W. Robertson.
S. Jervois Aarons, M.D.
Willmott Evans.
John Murray.
W. Adams Frost.
C. R. C. Lyster.
Samuel Noble Bruce.
Cuthbert Chapman Gibbes, M.D.
H. Stringfellow Pendlebury, M.B.
William Turner, M.B.
Alexander Crombie, M.D.
Thomas Herbert Kellock, M.D.
1899 Oswald Baker.
James Hugh Thursfield, M.D.
Lindley Marcroft Scott, M.D.
F. Rufenacht Walters, M.D.
Alfred P. Hillier, M.D.
Louis Bathe Rawling, M.B.
John Edward Sandiland, M.B.
Herbert Mundy.
Arthur J. Whiting, M.D.
W. H. Crosse, M.D.
Edward Farquhar Buzzard, M.B.
Greville Macdonald, M.D.
George Jones, M.B.

1899 Richard Harding Bremridge.
Herbert Campbell Thomson, M.D.
Thomas Morison Legge, M.D.
William John Ritchie Simpson, M.D.
Archibald Robert John Douglas, M.B., B.S.
Ernest Playfair, M.B.
Karl Fürth, M.D.
Purves Stewart, M.D.
1900 Clive Riviere, M.B.
H. Roe Walker.
Richard Lake.
Percy Flemming, M.D., B.S.
John Shields Fairbairn, M.B., B.Ch.
Hugh Lloyd Williams.
Aslett Baldwiu.
Walter Langdon Brown, M.B.
Charles Ryall.
William Hern.

1900 Cecil Huntington Leaf, M.B.
Edwin Harding Lendon, M.B.
Surg.-Gen. Henry Skey Muir, C.B.
Lieut.-Col. William Reid Murphy, D.S.O., I.M.S.
James Harry Sequeira, M.D.
Harold Batty Shaw, M.D.
Charles Herbert Thompson, M.D.
John William Thomson-Walker.
1901 Sir Hugh Reeve Beevor, Bart., M.D.
J. Brunton Blaikie, M.D.
John Patrick Henry, M.D.
Herbert John Paterson.
George Henkell Drummond Robinson, M.D.
Elmore Wright Brewerton.
Thomas Rupert Hampden Bucknal M.S., M.D.
William Douglas Harmer.
Harry George Plimmer.

The following Non-resident Fellows pay an annual subscription of £3 3s., and are thereby entitled to all the privileges of Resident Fellows.

Elected

1891 BRODIE, CHARLES GORDON, Fernhill, Wootton Bridge, Isle of Wight.

1884 DRAGE, LOVELL, M.D., B.Ch.Oxon., Burleigh Mead, Hatfield, Herts.

1897 GILFORD, HASTINGS, Norwood House, King's road, Reading. *Trans.* 1.

1873 PARKER, ROBERT WILLIAM, Senior Surgeon to the East London Hospital for Children; Senior Surgeon to the German Hospital; Caryll Hurst, West Grinstead, Sussex. C. 1888-9, 1899—1901. S. 1895-8. *Bldg. Com.* 1889-92. *Referee*, 1891-5. *Lib. Com.* 1885-87. 1892-5, 1898-9. *Ho. Com.* 1892-5, 1899—1901. *Trans.* 4.

1900 PRICE-JONES, CECIL, M.B., 7, Claremont road, Surbiton, Surrey.

1882 REID, THOMAS WHITEHEAD, M.D., Surgeon to the Kent and Canterbury Hospital; St. George's House, Canterbury.

1891 RUFFER, MARC ARMAND, M.D., The Quarantine Board, Alexandria.

1898 THOMAS, J. LYNN, C.B., Surgeon to the Cardiff Infirmary; Consulting Surgeon to the Hamadryad Hospital, Green-lawn, Pen-y-Lan, Cardiff.

1899 WOODHEAD, GERMAN SIMS, M.D., Professor of Pathology in the University of Cambridge; 6, Scrope terrace, Cambridge.

NON-RESIDENT FELLOWS

Elected

1866 *Allbutt, Thomas Clifford,* M.D., LL.D.Glasgow, F.R.S., Regius Professor of Physic, University of Cambridge; Consulting Physician to the Leeds General Infirmary; St. Rhadegund's, Cambridge. *Trans.* 8.

1884 *Anderson, Alexander Richard,* Surgeon to the General Hospital, 5, East Circus Street, Nottingham. *Trans.* 1.

1880 *Appleton, Henry,* M.D., 19, Regent terrace, Anlaby road, Hull.

1896 *Bagshawe, Frederic,* M.D., J.P., 35, Warrior Square, St. Leonard's-on-Sea.

1895 *Baldwin, Gerald R.,* 166, Victoria street, Melbourne, Australia.

1891 *Balgarnie, Wilfred,* M.B., The Dutch House, Hartley Wintney, Winchfield.

1896 *Ball, Charles Bent,* M.D., Ch.M., 24, Merrion square North, Dublin.

1866 *Banks, Sir John,* K.C.B., M.D., LL.D., D.Sc., Physician in Ordinary to H.M. the King in Ireland; Physician-to Richmond, Whitworth, and Hardwicke Hospitals; Regius Professor of Physic in the University of Dublin; 45, Merrion square, Dublin.

Elected

1886 *Banks, Sir William Mitchell*, M.D., Surgeon to the Liverpool Royal Infirmary; 28, Rodney street, Liverpool.

1900 *Bardswell, Noel Dean*, M.D., The Beacons, Surbiton, Surrey.

1882 *Barker, Frederick Charles*, M.D., Surgeon-Major, Bombay Medical Service.

1881 *Barnes, Henry*, M.D., LL.D., F.R.S. Ed., Physician to the Cumberland Infirmary; 6, Portland square, Carlisle.

1861 **Barnes**, *Robert*, M.D., Bernersmede, Eastbourne. C. 1877-8. V.P. 1889-90. *Referee*, 1867-76, 1891—. *Lib. Com.* 1869-73. *Sci. Com.* 1889—. *Trans.* 4.

1860 *Bealey, Adam*, M.D., M.A., Felsham Lodge, Felsham road, St. Leonard's-on-Sea, Sussex.

1896 *Belben, Frank*, M.B., Endsleigh, Suffolk road, Bournemouth.

1880 *Bennett, Alexander Hughes*, M.D. (Travelling).

1889 *Bentley, Arthur J. M.*, M.D., Mena House, Pyramids, Cairo, Egypt.

1872 *Beverley, Michael*, M.D., Consulting Surgeon to the Norfolk and Norwich Hospital; 54, Prince of Wales road, Norwich.

1865 *Bickersteth, Edward Robert*, Consulting Surgeon to the Liverpool Royal Infirmary; 2, Rodney street, Liverpool. *Trans.* 1.

1892 *Bickersteth, Robert Alexander*, M.A., M.B., Assistant Surgeon to the Liverpool Royal Infirmary; 2, Rodney street, Liverpool.

1849 **Birkett**, *Edmund Lloyd*, M.D., Consulting Physician to the City of London Hospital for Diseases of the Chest; Westbourne Rectory, Emsworth, Hampshire. C. 1865-6. *Referee*, 1851-9.

1900 *Blake, William Henry*, M.D.Brux., Bedford Lodge, West Wickham, Kent.

Elected

1865 *Blanchet, Hilarion*, 35, Conillard street, Quebec, Canada.

1890 *Bostock, R. Ashton*, Surgeon, Scots Guards, Cefn Mor, Penmaen, Glamorganshire.

1869 *Bourne, Walter*, M.D. (Travelling).

1874 *Bradshaw, A. F.*, C.B., Surgeon Major-General, 111, Banbury road, Oxford.

1899 *Bradshaw, Thomas Robert*, M.D., 51, Rodney street, Liverpool. *Trans.* 2.

1900 *Braine-Hartnell, James Christopher Reginald*, Cotswold Sanatorium, Stroud, Glos.

1876 *Bridges, Robert*, M.B., Manor House, Yattendon, Newbury, Berks.

1867 *Bridgewater, Thomas*, M.B., LL.D., Harrow-on-the-Hill, Middlesex.

1891 *Brodie, Charles Gordon*, Fernhill, Wootton Bridge, Isle of Wight.

1892 *Bronner, Adolph*, M.D., Senior Surgeon to Bradford Eye and Ear Hospital; Laryngologist to Bradford Royal Infirmary; 33, Manor row, Bradford.

1894 *Brook, William Henry Breffit*, M.D., B.S., 8, Eastgate, Lincoln.

1899 *Brooksbank, Hugh Lamplugh*, M.B., B.C., Thornbarrow, Windermere.

1888 *Browne, Henry Langley*, Moor House, West Bromwich.

1881 *Browne, John Walton*, M.D., Surgeon to the Belfast Royal Hospital; Surgeon to the Belfast Ophthalmic Hospital; 10, College square N., Belfast.

1864 *Buckle, Fleetwood*, M.D., Merton Lodge, Merton road, Southsea.

1901 *Byrne, William Samuel*, M.D., Anne street, Brisbane, Queensland.

1851 *Cadge, William*, Consulting Surgeon to the Norfolk and Norwich Hospital; 49, St. Giles's street, Norwich. *Trans.* 1.

Elected

1891 *Campbell, Henry Johnstone*, M.D., 36, Manningham lane, Bradford.

1900 *Carlyon, Thomas Baxter*, 9, Royal Arsenal, Woolwich.

1875 *Carter, Charles Henry*, M.D., Consulting Physician to the Hospital for Women, Soho Square, 5, Homefield road, Bromley, Kent.

1888 *Carter, William Jeffreys Becher*, Aliwal North, Cape Colony.

1898 *Cave, Edward John*, M.D., Bath.

1884 *Chaffey, Wayland Charles*, M.D., Physician to the Royal Alexandra Hospital for Children; 13, Montpellier road, Brighton.

1885 *Chapman, Paul Morgan*, M.D., Physician to the Hereford General Infirmary, 1, St. John street, Hereford. *Trans.* 1.

1881 *Chavasse, Thomas Frederick*, M.D., C.M., Senior Surgeon to the Birmingham General Hospital; 22, Temple row, Birmingham. *Trans.* 3.

1873 *Chisholm, Edwin*, M.D., Abergeldie, Ashfield, near Sydney, New South Wales.

1892 *Clark, James Charles*, 35, Castle road, Bedford.

1897 *Clark, W. Gladstone*, 6, Nicholas street, Chester.

1857 *Coates, Charles*, M.D., Consulting Physician to the Bath Royal United Hospital; 10, Circus, Bath.

1893 *Cole, Robert Henry*, M.D., Moorcroft, Hillingdon, Uxbridge.

1891 *Cook, Herbert George*, M.D., B.S., 22, Newport road, Cardiff.

1899 *Corrigan, William Jenkinson*, Cloughmore, Splott avenue, Cardiff.

1891 *Coumbe, John Batten*, M.D., 55, High street, Lowestoft.

1869 *Cresswell, Pearson R.*, C.B., Senior Surgeon to the Merthyr General Hospital; Dowlais, Merthyr Tydfil.

Elected

1892 *Cross, Francis Richardson*, M.B., Ophthalmic Surgeon to the Bristol Royal Infirmary, and Surgeon to the Bristol Eye Hospital; Worcester House, Clifton, Bristol.

1895 *Dardel, Jean*, M.D., Aix-les-Bains, Savoy.

1879 *Darwin Francis*, M.B., F.R.S., Wychfield, Huntingdon road, Cambridge.

1874 *Davidson, Alexander*, M.D., Consulting Physician to the Liverpool Royal Infirmary; Emeritus Professor, University College, Liverpool; 2, Gambier terrace, Liverpool.

1878 *Davy, Richard*, Consulting Surgeon to the Westminster Hospital; Burstone House, Bow, North Devon. *Trans.* 1.

1882 *Dawson, Yelverton*, M.D., Heathlands, Southbourne-on-Sea, Hants.

1889 *Delépine, Sheridan*, B.Sc., M.B., C.M., Professor of Pathology, Owens College, Manchester. *Trans.* 1.

1867 *Drage, Charles*, M.D., Hatfield, Herts.

1884 *Drage, Lovell*, M.D.Oxon., Burleigh Mead, Hatfield, Herts.

1898 *Dreschfeld, Julius*, Farndon House, Rusholme, Manchester.

1885 *Drummond, David*, M.D., 7, Saville place, Newcastle-on-Tyne.

1880 *Drury, Charles Dennis Hill*, M.D., Bondgate, Darlington.

1899 *Drury, Edward Guy Dru*, M.B., B.S., Grahamstown, South Africa.

1871 *Dukes, Clement*, M.D., B.S., Physician to Rugby School, and Senior Physician to the Hospital of St. Cross, Rugby; Sunnyside, Rugby, Warwickshire.

1867 *Dukes, Major Charles*, M.D., Clarence Villa, Torrs park, Ilfracombe, North Devon.

1889 *Duncan, John*, M.D., St. Petersburg, Russia.

Elected

1872 *Eager, Reginald*, M.D., Northwoods, near Bristol.

1887 *Easmon, John Farrell*, M.D., Assistant Colonial Surgeon, Gold Coast Colony, and Acting Chief Medical Officer of the Colony; Accra, Gold Coast, West Africa.

1887 *Elliott, John*, 24, Nicholas street, Chester.

1868 *Ellis, James*, M.D., The Sanatorium, Anaheim, Los Angeles County, California.

1889 *Elliston, William Alfred*, M.D., Stoke Hall, Ipswich.

1875 *Fagan, John*, Consulting Surgeon to the Belfast Royal Hospital; 20, Fitzwilliam place, Dublin.

1897 *Fagge, Thomas Henry*, M.D., Villa de la Porte Rouge, Monte Carlo.

1869 *Fairbank, Frederick Royston*, M.D., Westcott, Dorking.

1872 *Fenwick, John C. J.*, M.D., Physician to the Durham County Hospital; Long Framlington, Morpeth.

1879 *Finlay, David White*, M.D., Professor of the Practice of Medicine in the University of Aberdeen; Physician and Lecturer on Clinical Medicine to the Aberdeen Royal Infirmary; Consulting Physician to the Royal Hospital for Diseases of the Chest, London; 2, Queen's terrace, Aberdeen. *Referee*, 1891-3. *Trans.* 2.

1864 *Folker, William Henry*, Consulting and late Hon. Surgeon to the North Staffordshire Infirmary; Bedford House, Hanley, Staffordshire.

1896 *Forestier, Henri*, M.D., Aix-les-Bains, Savoie, France.

1892 *Foster, Michael George*, M.A., M.B., Villa Camilla, San Remo.

1859 *Fox, Edward Long*, M.D., Consulting Physician to the Bristol Royal Infirmary; Church House, Clifton, Gloucestershire.

1884 *Franks, Kendal*, M.D., c/o J. H. Franks, Esq., C.B., Dalriada, Blackrock, Co. Dublin. *Trans.* 2.

1876 *Furner, Willoughby*, M.D., Surgeon to the Sussex County Hospital; Brunswick square, Brighton.

Elected

1864 *Gairdner, Sir William Tennant*, M.D., K.C.B., LL.D., F.R.S., Honorary Physician in Ordinary to H.M. the King in Scotland; formerly Professor of the Practice of Medicine in the University of Glasgow; Honorary Consulting Physician to the Western Infirmary, Glasgow; 32, George square, Edinburgh. *Trans.* 1.

1885 *Gamgee, Arthur*, M.D., F.R.S., Emeritus Professor of Physiology in the Owens College, Victoria University, Manchester; Montreux, Switzerland.

1867 *Garland, Edward Charles*, Yeovil, Somerset.

1879 *Garstang, Thomas Walter Harropp*, Englefield, Delamer road, Bowdon, Cheshire.

1889 *Gaskell, Walter Holbrook*, M.D., F.R.S., Lecturer on Physiology, University of Cambridge; The Uplands, Great Shelford, Cambs.

1864 *Gibbes, Heneage*, M.D., Health Officer, Detroit, Michigan, U.S.A.

1897 *Gibson, George Alexander*, M.D., D.Sc., 3, Drumsheugh Gardens, Edinburgh.

1897 *Gilford, Hastings*, Norwood House, King's road, Reading. *Trans.* 1.

1893 *Gordon, William*, M.B., M.C., The Old Rectory, Goring-on-Thames, Oxon.

1890 *Gordon, William*, M.D., Barnfield Lodge, Exeter.

1898 *Gray, J. A.*, M.B., Wadham Lodge, Uxbridge road, Ealing.

1889 *Greene, George Edward Joseph*, M.A., D.Sc., F.L.S., Monte Vista, Ferns, County Wexford.

1875 *Greenfield, William Smith*, M.D., Professor of Pathology and Clinical Medicine in the University of Edinburgh; 7, Heriot row, Edinburgh. *Sci. Com.* 1879. *Referee*, 1881.

1900 *Greer, William Jones*, 2, Chepstow road, Newport, Mon.

1882 *Gresswell, Dan Astley*, M.A., M.D., D.P.H., Chairman, Board of Public Health, Melbourne, Victoria.

Elected

1889 *Griffiths, Joseph*, M.A., M.D., C.M., Reader in Surgery in the University of Cambridge; Surgeon to Addenbrooke's Hospital; 63, Trumpington street, Cambridge. *Pro.* 1.

1870 *Hamilton, Robert*, Consulting Surgeon to the Royal Southern Hospital, Liverpool; Magherabuoy, Portrush, Co. Antrim, Ireland.

1864 **Harley**, *John*, M.D., F.L.S., Hon. Physician to St. Thomas's Hospital; Consulting Physician to the London Fever Hospital; Beeding, Pulborough, Sussex. S. 1875-7. C. 1879-80. V.P. 1895-7. *Referee*, 1871-4, 1882-95. *Sci. Com.* 1879. *Trans.* 10.

1892 *Harsant, William Henry*, Surgeon to the Bristol Royal Infirmary; The Tower House, Clifton road, Clifton, Bristol.

1854 *Haviland, Alfred*, Ridgemount, Frimley Green, Surrey.

1890 *Haviland, Frank Papillon*, M.D., B.C., 57, Warrior square, St. Leonard's-on-Sea.

1885 *Hawkins, Francis Henry*, M.D., Physician to the Royal Berkshire Hospital; 73, London street, Reading. *Trans.* 1.

1900 *Hayford, Ernest James*, M.D., Free Town, Sierra Leone.

1860 **Hayward**, *Henry Howard*, Consulting Surgeon Dentist to St. Mary's Hospital; Harbledown, 120, Queen's road, Richmond. C. 1878-9.

1861 *Hayward, William Henry*, Oxford road, Burnley, Lancashire.

1899 *Hind, Henry*, Harrogate.

1900 *Hobhouse, Edmund*, M.D., 36, Brunswick place, Brighton.

1843 **Holden**, *Luther*, Consulting Surgeon to St. Bartholomew's Hospital, Pinetoft, Ipswich. C. 1859. L. 1865. V.P. 1874. *Referee*, 1866-7. *Lib. Com.* 1858.

1894 *Holland, James Frank*, M.D., St. Moritz, Engadine, Switzerland.

Elected

1868 *Hollis, William Ainslie*, M.D., Physician to the Sussex County Hospital; 1, Palmeira avenue, Hove. *Trans.* 1.

1881 *Howard, Henry*, M.B., Medical Officer of Health, Williamstown, Melbourne, Victoria.

1898 *Hulke, S. Backhouse*, Ivy House, Walmer, Kent.

1882 *Humphry, Laurence*, M.D., 3, Trinity street, Cambridge.

1847 *Image, William Edmund*, Herringswell House, Mildenhall, Suffolk. *Trans.* 1.

1883 *Jenkins, Edward Johnstone*, M.D., The Australian Club, Sydney, New South Wales.

1881 *Jennings, William Oscar*, M.D., 74, Avenue Marceau, Paris.

1901 *Johnson, Edward Angas*, M.B., St. Catharine's, Prospect, South Australia.

1889 *Johnson, Harold J.*, Senior Assistant, Gloucester County Asylum, Gloucester.

1848 *Johnstone, Athol Archibald Wood*, Consulting Surgeon to the Royal Alexandra Hospital for Sick Children, St. Moritz House, 61, Dyke road, Brighton. *Lib. Com.* 1860. *Trans.* 1.

1876 *Jones, Leslie Hudson*, M.D., Limefield House, Cheetham hill, Manchester.

1875 *Jones, Philip Sydney*, M.D., Consulting Surgeon to the Sydney Infirmary; 10, College street, Sydney, New South Wales. [Agents: Messrs. D. Jones & Co., Wool Exchange, Coleman Street, E.C.]

1865 *Jordan, Furneaux*, Consulting Surgeon to the Queen's Hospital, Birmingham; Harborne, near Birmingham.

1872 *Kelly, Charles*, M.D., Ellesmere, Gratwicke road, Worthing, Sussex.

1848 *Kendell, Daniel Burton*, M.B., Thornhill House, Walton, near Wakefield, Yorkshire.

1890 *Kerr, J. G. Douglas*, M.B., C.M., 6, The Circus, Bath.

Elected

1884 *Keser, Jean Samuel,* M.D., Villa St. Martin, Vevey, Switzerland.

1877 *Khory, Rustomjee Naserwanjee,* M.D.Brux., Hormazd Villa, Khumballa hill, Bombay.

1898 *Klefstad-Sillonville, O.,* M.D., Aix-les-Baine, Savoie.

1888 *Kynsey, Sir William Raymond,* C.M.G., Oriental Club, Hanover square. (Travelling.)

1889 *Lancaster, Ernest le Cronier,* M.B., B.Ch., Assistant Physician to the Swansea Hospital; Hon. Physician to the Swansea and South Wales Institution for the Blind; Winchester House, Swansea, S. Wales.

1873 *Larcher, O.,* M.D., Laureate of the Institute of France, of the Medical Faculty, and Academy of Paris, &c.; 97, Rue de Passy, Passy, Paris.

1862 *Latham, Peter Wallwork,* M.D., Downing Professor of Medicine, Cambridge University, 1874–94; Senior Physician to Addenbrooke's Hospital, Cambridge; 17, Trumpington street, Cambridge.

1880 *Laycock, George Lockwood,* M.B., C.M., Melbourne, Victoria, Australia.

1892 *Lazarus-Barlow, Walter Sydney,* M.D., Cecil House, Cavendish road, Sutton, Surrey. *Sci. Com.* 1892—.

1886 *Lediard, Henry Ambrose,* M.D., Surgeon to the Cumberland Infirmary; 35, Lowther street, Carlisle. *Trans.* 1.

1882 *Ledwich, Edward l'Estrange,* Anatomist to the Royal College of Surgeons, Ireland; 80, Upper Fitzwilliam street, Dublin.

1883 *Leeson, John Rudd,* M.D., C.M., Clifden House, Twickenham.

1869 *Legg, John Wickham,* M.D. C. 1886. *Referee,* 1882-5. *Lib. Com.* 1878-85. *Trans.* 2.

1898 *Lindsay, James,* M.A., M.D., 13, College square east, Belfast.

Elected

1872 ***Little, David,*** M.D., Senior Surgeon to the Royal Eye Hospital, Manchester; Ophthalmic Surgeon to the Manchester Royal Infirmary; Lecturer on Ophthalmology at the Victoria University; 21, St. John street, Manchester.

1889 ***Little, James,*** M.D., Physician to the Adelaide Hospital; 14, Stephen's Green North, Dublin.

1871 ***Little, Louis Stromeyer,*** Shanghai, China.

1894 ***Lowe, Thomas Pagan,*** 16, The Circus, Bath.

1889 ***MacAlister, Donald,*** M.A., B.Sc., M.D., Physician to Addenbrooke's Hospital; Linacre Lecturer and Tutor, St. John's College; University Lecturer in Medicine; St. John's College, Cambridge.

1887 ***Macdonald, George Childs,*** M.D.

1866 ***Macgowan, Alexander Thorburn,*** M.D., Vyvian House, Clifton park, Bristol.

1859 ***M'Intyre, John,*** M.D., LL.D., Odiham, Hants.

1876 ***Mackey, Edward,*** M.D., Physician to the Sussex County Hospital; Senior Physician to the Royal Alexandra Hospital for Sick Children; 56, Lansdowne place, Brighton.

1854 ***Mackinder, Draper,*** M.D., 26, Denmark Villas, Hove, Sussex.

1893 ***MacLeod, Surgeon-Colonel Kenneth,*** M.D., The Towers, Woolston, S. Hants.

1891 ***Manby, Alan Reeve,*** M.V.O., M.D., Surgeon Apothecary to His Majesty's Household at Sandringham and to T.R.H. the Prince and Princess of Wales at Sandringham; East Rudham, Norfolk.

1894 ***Marriott, Charles William,*** M.D., Aubrey House, Bath road, Reading.

1892 ***Martin, Christopher,*** M.B., C.M., Surgeon to the Birmingham and Midland Hospital for Women; 35 George road, Edgbaston, Birmingham.

Elected

1899 *Martyn, Gilbert John King*, M.D., 8, Gay street, Bath.

1883 *Maudsley, Henry Carr*, M.D., 22, Collins street, Melbourne, Victoria.

1839 *Meade, Richard Henry*, Consulting Surgeon to the Bradford Infirmary; Bradford, Yorkshire. *Trans.* 1.

1897 *Merry, William Joseph Collings*, M.D., B.Ch., 2, Chiswick place, Eastbourne.

1898 *Millard, William Joseph Kelson*, M.D., 7, Bayshill villas, Cheltenham.

1895 *Mills-Roberts, Robert Herbert*, Hafod-ty, Llanberis, North Wales.

1887 *Mivart, Frederick St. George*, M.D., Local Government Board Inspector; 6, Edge hill, Wimbledon.

1896 *Moore, Sir John*, M.D., 40, Fitzwilliam square west, Dublin.

1891 *Morris, Graham*, Wallington, Surrey.

1894 *Morse, Thomas Herbert*, All Saints' Green, Norwich. *Trans.* 1.

1881 *Nall, Samuel*, M.B., Dryhurst Lodge, Disley, Stockport.

1889 *Napier, Francis Horatio*, M.B., Cape Town.

1870 *Neild, James Edward*, M.D., Lecturer on Forensic Medicine and Psychological Medicine in the University of Melbourne; 21, Spring street, Melbourne, Victoria.

1895 *Newsholme, Arthur*, M.D., 11, Gloucester place, Brighton.

1868 *Nicholls, James*, M.D., Trekenning House, St. Columb, Cornwall.

1849 *Norman, Henry Burford*, The Manor-house, Drayton, Taunton, Somerset. *Lib. Com.* 1857.

1847 *Nourse, William Edward Charles*, Norfolk Lodge, Thurloe road, Torquay.

1884 *Oakes, Arthur*, M.D., Narrabri, Cole Park road, Twickenham.

1880 *O'Connor, Bernard*, A.B., M.D., Senior Physician to the North London Hospital for Consumption; 25, Hamilton road, Ealing.

1896 *Ogle, John Gilbert*, M.D., South Redlands, Reigate.

Elected

1855 *Ogle, William*, M.A., M.D., Consulting Physician to the Royal Derbyshire Infirmary; The Elms, Duffield road, Derby.

1870 *Oldham, Charles Frederic*, India [Agents: Messrs. Grindlay and Co., 55, Parliament street].

1896 *Oliver, George*, M.D., Riversleigh, Farnham, Surrey, and Harrogate.

1883 *Oliver, Thomas*, M.A., M.D., Professor of Physiology, University of Durham; and Physician to the Newcastle-on-Tyne Infirmary; 7, Ellison place, Newcastle-on-Tyne. *Trans.* 1.

1871 *O'Neill, William*, M.D., C.M., late Physician to the Lincoln Lunatic Hospital, and Physician, Lincoln General Dispensary, &c.; 2, Lindum road, Lincoln.

1890 *Ord, William Wallis*, M.D., The Hall, Salisbury.

1885 *Ormsby, L. Hepenstal*, M.D., Lecturer on Clinical and Operative Surgery and Surgeon to the Meath Hospital and County Dublin Infirmary; Surgeon to the Children's Hospital, Dublin; 92, Merrion square west, Dublin.

1887 *Paget, Charles Edward*, Medical Officer of Health to the County Council of Northamptonshire; County Hall, Northampton.

1858 *Paley, William*, M.D., Physician to the Ripon Dispensary; Yore Bank, Ripon, Yorkshire.

1887 *Pardington, George Lucas*, M.D., 47, Mount Pleasant road, Tunbridge Wells.

1873 *Parker, Robert William*, Senior Surgeon to the East London Hospital for Children; Senior Surgeon to the German Hospital; Caryll Hurst, West Grinstead, Sussex. C. 1888-9, 1899—1901. S. 1895-8. *Bldg. Com.* 1889-92. *Referee*, 1891-5. *Lib. Com.* 1885-87, 1892-5, 1898-9. *Ho. Com.* 1892-5, 1899—1901. *Trans.* 4.

1885 *Parker, Rushton*, M.B., B.S., Professor of Surgery, University College, Liverpool (Victoria University); Surgeon to the Liverpool Royal Infirmary; 59, Rodney street, Liverpool.

Elected

1891 *Parkin, Alfred*, M.S., M.D., 24, Albion street, Hull. *Trans.* 1.

1879 *Peel, Robert*, 120, Collins street east, Melbourne, Victoria.

1874 *Penhall, John Thomas*, The Cedars, Broadwas-on-Teme, Worcester.

1897 *Perram, Charles Herbert*, M.D., 55, Bromham Road, Bedford.

1879 *Pesikaka, Hormasji Dosabhai*, 43, Hornby road, Bombay.

1878 *Philipson, Sir George Hare*, M.D., D.C.L., Professor of Medicine in Durham University; Consulting Physician to the Newcastle-upon-Tyne Royal Infirmary; 7, Eldon square, Newcastle-upon-Tyne.

1891 *Pierce, Bedford*, M.D., The Retreat, York.

1897 *Pigg, T. Strangeways*, 62, Jesus Lane, Cambridge.

1841 **Pitman**, *Sir Henry Alfred*, M.D., Consulting Physician to St. George's Hospital; Cranbrook, Byculiah park, Enfield. L. 1851-3. C. 1861-2. T. 1863-8. V.P. 1870-1. *Referee*, 1849-50. *Lib. Com.* 1847.

1892 *Powell, Herbert Andrews*, M.A., M.D., M.Ch., Piccards Rough, Guildford.

1900 *Price-Jones, Cecil*, M.B., 7, Claremont road, Surbiton, Surrey.

1897 *Quartey-Papafio, Benjamin William*, M.D., Accra, Gold Coast, West Africa.

1857 *von Ranke, Henry*, M.D., 3, Sophienstrasse, Munich.

1890 *Ransom, William Bramwell*, M.D., Physician to the Nottingham General Hospital; The Pavement, Nottingham. *Trans.* 1.

1854 *Ransom, William Henry*, M.D., F.R.S., Consulting Physician to the Nottingham General Hospital; 17, Park Valley, Nottingham. *Trans.* 1.

1882 *Reid, Sir James*, Bart., G.C.V.O., K.C.B., M.D., Resident Physician and Physician in Ordinary to H.M. the King, Windsor Castle.

Elected

1884 *Reid, Thomas Whitehead*, M.D., Surgeon to the Kent and Canterbury Hospital; St. George's House, Canterbury, Kent.

1901 *Reissmann, Charles Henry*, M.B., B.C., B.Sc., Knutsford, Glenelg, South Australia.

1881 *Rice, George*, M.B., C.M., Sutton, Surrey.

1889 *Rivers, W. H. Rivers*, M.D., St. John's College, Cambridge.

1871 *Roberts, David Lloyd*, M.D., F.R.S.E., Consulting Obstetric Physician to the Manchester Royal Infirmary; Physician to St. Mary's Hospital, and Lecturer on Clinical Obstetrics and Gynæcology at the Owens College, Manchester; 11, St. John street, Manchester.

1889 *Roberts, Leslie*, M.D., 46, Rodney street, Liverpool.

1873 *Robertson, William Henry*, M.D., Consulting Physician to the Buxton Bath Charity and Devonshire Hospital; Buxton, Derbyshire.

1888 *Robinson, Frederick William*, M.D., C.M., Huddersfield.

1889 *Robson, Arthur William Mayo*, Professor of Surgery, Yorkshire College; Senior Surgeon, Leeds General Infirmary; 7, Park square, Leeds. *Trans.* 4. *Pro.* 1.

1885 *Rockwood, William Gabriel*, M.D., Colombo, Ceylon.

1898 *Rogers, Leonard*, I.M.S. [care of Messrs. Watson & Co., Calcutta.] *Trans.* 2.

1863 *Rowe, Thomas Smith*, M.D., Consulting Surgeon to the Royal Sea-Bathing Infirmary; Union crescent, Margate, Kent.

1891 *Ruffer, Marc Armand*, M.D., The Quarantine Board, Alexandria.

1898 *Salter, A.*, M.D., The Poplars, Sudbury, Harrow.

1855 **Sanderson**, *Sir John Burdon, Bart.*, M.D., LL.D., D.C.L.Durham, D.Sc., F.R.S., Regius Professor of Medicine in the University of Oxford; 64, Banbury road, Oxford. C. 1869-70. V.P. 1882. *Referee*, 1867-8, 1876-81. *Sci. Com.* 1862, 1870. *Lib. Com.* 1876-81. *Trans.* 2.

Elected

1867 *Sandford, Folliott James*, M.D., V.D., late Surgeon-Major, 2nd Batt. S.V.L.Infy., now Hon. Surgeon-Major; Surgeon to the Market Drayton Dispensary, and Consulting Physician to the Market Drayton Cottage Hospital ; Market Drayton, Shropshire.

1886 *Saundby, Robert*, M.D., LL.D., Physician to the General Hospital, and Consulting Physician to the Hospital for Women, and to the Eye Hospital, Birmingham ; Professor of Medicine, Mason University College; 140B, Great Charles street, Birmingham.

1891 *Saunders, Frederick William*, M.B., B.C., Chieveley House, near Newbury, Berks.

1883 *Schäfer, Edward Albert*, LL.D., F.R.S., Professor of Physiology in the University of Edinburgh. C. 1899-1900. *Referee*, 1888-99. *Sci. Com.* 1889—.

1861 *Scott, William*, M.D., Senior Physician to the Huddersfield Infirmary ; Waverley House, Huddersfield.

1897 *Semple, Edward*, M.D., Grove house, Fenstanton, Hunts.

1897 *Seymour, Surg.-Major Charles*, Bareilly, North-West Provinces, India.

1899 *Shuttleworth, George Edward*, M.D., Ancaster House, Richmond Hill.

1887 *Sidebotham, Edward John*, M.B., Erlesdene, Bowdon, Cheshire.

1857 *Siordet, James Lewis*, M.B., Villa Cabrolles, Mentone, Alpes Maritimes, France.

1896 *Sloane, John Stretton*, M.B., B.S., B.Sc., 7, Highfield street, Leicester.

1891 *Smith, G. Cockburn*, M.D., 29, Lansdown crescent, Cheltenham.

1886 *Smith, Howard Lyon*, Buckland House, Buckland Newton, Dorchester.

1894 *Smith, Robert Shingleton*, M.D., B.Sc., Deepholm, Clifton Park, Clifton, Bristol.

1894 *Smith, Thomas Rudolph*, M.B., B.C., Blytheholm, Stockton-on-Tees.

Elected

1868 *Solly, Samuel Edwin*, Colorado Springs, Colorado, U.S.A.

1899 *Stephen, Guy Neville*, Foreign Office Medical Staff.

1896 *Stephens, John William Watson*, M.B., B.C., Pathological Laboratory, Cambridge.

1891 *Stevens, Surg.-Capt. Cecil Robert*, M.B., B.S., I.M.S., Eden Hospital, Calcutta.

1854 *Stevens, Henry*, M.D., late Inspector, Medical Department, Local Government Board, Whitehall; Durham Lodge, St. Margaret's road, Twickenham.

1884 *Stewart, Edward*, M.D., Brook House, East Grinstead.

1879 *Stirling, Edward Charles*, M.D., Senior Surgeon to the Adelaide Hospital; Lecturer on Physiology in the University of Adelaide, South Australia [care of Messrs. Elder and Co., 7, St. Helen's place].

1871 *Strong, Henry John*, M.D., J.P., Consulting Surgeon to the Croydon General Hospital; Colonnade House, The Steyne, Worthing.

1890 *Sympson, E. Mansel*, M.D., B.C., Surgeon to the Lincoln County Hospital; Deloraine Court, Lincoln.

1886 *Teale, Thomas Pridgin*, M.B., F.R.S., Consulting Surgeon to the Leeds General Infirmary; 38, Cookridge street, Leeds.

1898 *Thomas, J. Lynn*, C.B., Surgeon to the Cardiff Infirmary; Consulting Surgeon to the Hamadryad Hospital; Green Lawn, Pen-y-lan, Cardiff.

1890 *Thomas, William Robert*, M.D., Little Forest, Bath road, Bournemouth.

1891 *Thomson, John Roberts*, M.D., Monkchester, Bournemouth.

1876 *Thornton, J. Knowsley*, M.B., C.M., Consulting Surgeon to the Samaritan Free Hospital for Women and Children; Hildersham Hall, Cambridge. C. 1891. *Lib. Com.* 1886-90, 1893-95. *Trans.* 5.

1883 *Thursfield, Thomas William*, M.D., Physician to the Warneford and South Warwickshire General Hospital; Selwood, Beauchamp square, Leamington.

Elected

1880 *Tivy, William James*, 8, Lansdowne place, Clifton, Bristol.

1871 *Trend, Theophilus W.*, M.D., 1, Grosvenor square, Southampton.

1881 *Treves, William Knight*, Surgeon to the National Hospital for Scrofula; 31, Dalby square, Cliftonville, Margate.

1867 *Trotter, John William*, formerly Surgeon-Major, Coldstream Guards; 4, St. Peter's terrace, York.

1873 *Turner, George Brown*, M.D., Camden House, Hemel Hempsted, Herts.

1894 *Turner, Philip Dymock*, M.D., Sudbury, Isle of Wight.

1891 *Tweed, Reginald*, M.D., Hembury Fort Cross, Honiton, Devon.

1881 *Tyson, William Joseph*, M.D., Senior Medical Officer of the Victoria Hospital, Folkestone; 10, Langhorne Gardens, Folkestone.

1900 *Uhthoff, John Caldwell*, M.D., Wavertree House, Hove, Brighton.

1867 Vintras, *Achille*, M.D., late Physician to the French Embassy and Senior Physician to the French Hospital and Dispensary, Shaftesbury avenue; De Courcel road, Brighton.

1854 *Waddington, Edward*, Hamilton, Auckland, New Zealand.

1868 *Walker, Robert*, Clovelly, Bideford.

1867 *Wallis, George*, Consulting Surgeon to Addenbrooke's Hospital; 6, Hills road, Cambridge.

1883 *Walters, James Hopkins*, Surgeon to the Royal Berkshire Hospital; 15, Friar street, Reading.

1899 *Warde, Wilfred Brougham*, M.D., 13, Lonsdale Gardens, Tunbridge Wells.

1846 *Ware, James Thomas*, Tilford House, near Farnham, Surrey.

1861 *Waters, A. T. Houghton*, M.D., Consulting Physician to the Royal Infirmary; 69, Bedford street, Liverpool. *Trans.* 3.

Elected

1874 *Wells, Harry*, M.D., San Ysidro, Buenos Ayres, S. America.

1882 *Wharry, Charles John*, M.D., 14, Ewell road, Surbiton, Surrey.

1897 *White, Charles Powell*, 2, Blandford Gardens, Woodhouse lane, Leeds.

1881 *Whitehead, Walter*, F.R.S. Ed., Senior Surgeon to the Manchester Royal Infirmary, Manchester and Salford Lock Hospital, and Manchester and Salford Skin Hospital; Professor of Clinical Surgery, Owens College, Victoria University; 499, Oxford road, Manchester. *Trans.* 1.

1885 *Whitla, William*, M.A., M.D., Professor of Materia Medica and Therapeutics, Queen's College, Belfast; Physician to, and Lecturer in Medicine at, the Belfast Royal Hospital; Consulting Physician to the Ulster Hospital for Women and Children; Consulting Physician to the Belfast Ophthalmic Hospital; 8, College square north, Belfast.

1870 *Wilkin, John F.*, M.D., Rose Ash Court, South Molton, Devon.

1883 *Willans, William Blundell*, Much Hadham, Herts.

1896 *Williams, Alfred Henry*, M.D., Rotorua, Harrow.

1859 *Williams, Charles*, Senior Surgeon to the Norfolk and Norwich Hospital; 48, Prince of Wales road, Norwich.

1887 *Wilson, Arthur Hervey*, M.D., 504, Broadway, Boston, U.S.A.

1889 *Wise, A. Tucker*, M.D., Montreux, Switzerland.

1850 *Wise, Robert Stanton*, M.D., Consulting Physician to the Southam Eye and Ear Infirmary; Beech Lawn, Banbury.

1885 *Wolfenden, Richard Norris*, M.D., Rangemont, Seaford, Sussex.

1892 *Woodhead, German Sims*, M.D., Professor of Pathology in the University of Cambridge; 6, Scrope terrace, Cambridge.

Elected

1879 *Woodward, G. P. M.*, M.D., Deputy Surgeon-General; 157, Liverpool street, Hyde Park, Sydney, New South Wales.

1892 *Wright, Almroth Edward*, M.D., Ch.B., Oakhurst, Netley, Hants.

1899 *Wynter, Andrew Ellis*, M.D., Corner House, Beckenham, Kent.

ANNUAL MEETING.

March 1st, 1901, *at* 5 *p.m.*

F. W. Pavy, M.D., LL.D., F.R.S., President.

Sir Thomas Barlow, Bart., M.D., A. Pearce Gould, M.S., } Hon. Secs.

Dr. S. Coupland and Dr. G. Eastes were appointed scrutineers of the ballot.

The minutes of the last meeting were read and signed.

Mr. Pearce Gould (Hon. Sec.) read the Report of the Council.

Report of the Council.

During the past year the Society has suffered the loss of its Patron, Her late Majesty Queen Victoria. At a Special General Meeting held on February 5th, a loyal address of condolence and congratulation to His Majesty, King Edward VII, was adopted with a dutiful request that he would extend to the Society His Royal Patronage. This address has been engrossed and presented.

Since March 1st, 1900, we have lost 21 Fellows by death, and 3 by resignation, and we have elected 30 new Fellows. Our numbers, therefore, stand as follows:

Honorary Fellows	6
Foreign Fellows	16
Resident Fellows	537
Non-resident Fellows	286
Total . . .	845

The Council has made several important changes in the method of dealing with papers since its last Report. It has ceased to publish the 'Proceedings' and to print the abstracts of papers to be read. It has added to the 'Transactions' reports of the discussions which have followed the reading of papers. At the same time it has allowed the authors of papers to publish them in medical and scientific journals without losing their privilege of publication in the Society's 'Transactions,' and it has decided that all papers accepted for reading before the Society shall be published in the 'Transactions.' The alterations in the Bye-laws and Standing Orders necessitated by these changes in practice have been duly made by the Society at a Special Meeting and by the Council. The result of these changes has up to the present time been quite satisfactory, and it is believed they will greatly add to the usefulness of the Society, and also effect a substantial economy.

The following Reports have been received:

1. *Report of the Honorary Treasurers.*

"The income of the Society during the past year has been £178 13*s.* 9*d.* more, and the expenditure £408 0*s.* 4*d.* less than in the year 1899. During the same period the assets have been increased by £312 8*s.* 1*d.*, and the Debenture Debt has been reduced by £300. The surplus of Assets over Liabilities now stands at £27,084 4*s.* 8*d.*

"The financial position of the Society will therefore be seen to be sound. Nevertheless in view of the loss in 1904 of the Berners Street rent (£436 10*s.* per annum), the Treasurers feel that it is desirable to effect, if possible, some further economies, and they are glad the matter is under the consideration of the Council."

2. *Report of the Honorary Librarians.*

"The Honorary Librarians have pleasure in reporting that an unusually large number of books have been added to the Library during the past year: by purchase 496, by donation 206,—in all 702. The Library has been most extensively used, upwards of 4000 volumes and journals have been borrowed during 1900; and the number of books borrowed from Lewis's Library has been much in excess of the usual number."

3. *Report of the Balneological and Climatological Committee.*

"The Reports on the Climates of England and Ireland have now all been handed in, and the Committee have therefore so far completed the work entrusted to them by the Society.

"The Report on Scotland they do not propose to undertake, since it has been found impossible to obtain any local assistance.

"The Council has requested the Committee to ascertain the probable cost of publishing their Report up to completion of the work."

Sir WILLIAM CHURCH (Senior Hon. Treasurer) read and explained the accounts, and the President moved that the Report of the Council, together with the Audited Statement of the Accounts, be adopted and printed in the next volume of the 'Transactions.' Carried *nem. con.*

The President then delivered the Annual Address (see page xcvii).

The usual votes of thanks to the retiring officers and members of Council were carried, and the President called

upon the Scrutineers to report the result of the ballot, as follows :

President.—Frederick William Pavy, M.D., LL.D., F.R.S.

Vice-Presidents.—Sydney Ringer, M.D., F.R.S. ; Charles Theodore Williams, M.D. ; Sir William Dalby ; Henry Morris, M.A., M.B.

Honorary Treasurers.—Sir William Selby Church, Bart., M.D. ; J. Warrington Haward.

Honorary Secretaries.—Sir Thomas Barlow, Bart., M.D. ; Clinton Thomas Dent.

Honorary Librarians.—Norman Moore, M.D. ; Rickman J. Godlee, M.S.

Members of Council.—Charles Edward Beevor, M.D. ; Francis de Havilland Hall, M.D. ; George Ernest Herman, M.B. ; Percy Kidd, M.D. ; William Hale White, M.D. ; Henry Edward Juler ; Charles R. B. Keetley ; Charles Barrett Lockwood ; Richard Clement Lucas, B.S., M.B. ; Thomas Laurence Read.

Income and Expenditure Account for the Year ending 31st December, 1900.

Expenditure

	£	s.	d.	£	s.	d.
Rent, Rates, and Taxes	166	11	3			
Salaries of Library Staff and Accountant	649	10	0			
Gratuity to Mr. Clarke	26	5	0			
House Servants, Cleaners, etc. ...	243	13	8			
Lighting, Warming, and Cleaning ...	271	15	5			
Printing and Stationery, Stamps and Telegrams	206	15	10			
Meeting Expenses	39	19	8			
Miscellaneous Disbursements ...	82	13	6			
				1687	4	4
Repairs, Alterations, Furniture, etc.				160	10	10
Interest on Debentures				1038	8	5
Depreciation of Library Purchases ...	222	10	1			
Depreciation of Fixtures, Fittings, etc.	61	3	9			
				283	13	10
'Transactions'				371	12	2
Law Charges				6	2	4
Audit Fee				10	10	0
**Balance, being excess of Income over Expenditure during the year* ...				769	13	0
				£4327	14	11

Income

	£	s.	d.	£	s.	d.
442 *Annual Subscriptions at* £3 3s.	1392	6	0			
87 *do.* £1 1s.	91	7	0			
				1483	13	0
Composition Fees				33	12	0
Entrance Fees				185	17	0
Rents Receivable				2543	2	8
Sale of 'Transactions'				67	5	5
Interest on New South Wales Stock ...				12	10	2
Miscellaneous Receipts				1	14	8
				£4327	14	11

Audited and approved,
TOM MUNDY,
Chartered Accountant.

14th February, 1901.

* This balance represents the difference between the Expenditure and Income of the year 1900; *not* the actual cash balance in the hands of the Treasurers.

(B) Statement of Liabilities and Assets, 31st December, 1900.

Liabilities.	£	s.	d.	£	s.	d.
3 per Cent. First Mortgage Debentures . . [The Debenture Debt has been reduced by £300 since the previous statement, by cash paid in respect to Debentures redeemed.]				34,500	0	0
Sundry Creditors				1,057	8	8
Debenture Interest not claimed . . .				9	13	3
Endowment Fund Account				5	5	0
[Surplus, 31st December, 1899	£26,314	11	8			
Add—						
Excess of Income over Expenditure, 1900 . .	769	13	0			
	£27,084	4	8]			
Balance, being Surplus of Assets over Liabilities				27,084	4	8
				£62,656	11	7

Assets.	£	s.	d.	£	s.	d.
Freehold and Leasehold Property (as per Balance-sheet of 31st December, 1899).				51,150	0	0
Fixtures, Fittings, and Furniture	£1,223	15	6			
Less 5 per cent. written off for depreciation . . .	61	3	9			
				1,162	11	9
Engravings . . . . . (as per Balance-sheet of 31st December, 1899).				555	0	0
Contents of Library as on December 31st, 1899 . .	8,313	17	0			
Added in 1900 . £445 0 3						
Less depreciation (50 per cent.) 222 10 1						
	222	10	2			
				8,536	7	2
Stock of 'Climates and Baths' .				137	19	6
Investment—"Permanent Endowment Fund" . . . (New South Wales 4 per Cent. Inscribed Stock).				326	7	3
Sundry Debtors for Rents . .				457	13	3
Cash at Bank (Debenture Account)				9	13	3
Cash at Bank and in hand .				320	19	5
				£62,656	11	7

NOTE.—The Society is also possessed of £623 14*s.* 10*d.* Consols, but as the sum in question is held in trust for a specific purpose, viz. the Marshall Hall Memorial Prize Fund, the capital sum has not been included amongst the assets of the Society.

Audited and approved,

TOM MUNDY,

Chartered Accountant.

14th February, 1901.

(C) Statement of Cash Receipts and Payments for the Year ending 31st December, 1900.

Receipts

	£	s.	d.	£	s.	d.	£	s.	d.
Balance 1st January, 1900 ...							486	9	0
Subscriptions, Fees, &c.:									
Annual Subscriptions at £3 3s....	1397	11	0						
Annual Subscriptions at £1 1s.	92	8	0						
Composition Fees (Life)	33	12	0						
Entrance Fees	185	17	0						
				1709	8	0			
Sales of 'Climates and Baths' ...				0	10	6			
'Transactions':									
Sold by Messrs. Longmans	60	7	1						
„ Mr. H. K. Lewis	2	4	8						
„ Resident Librarian	4	13	8						
				67	5	5			
Rents				2188	15	8			
Interest:									
On Permanent Endowment Fund				12	10	2			
Miscellaneous Receipts ...				8	1	2			
							3986	10	11
							£4472	19	11

14th February, 1901.

Payments

	£	s.	d.	£	s.	d.
Rent, Taxes, Rates, &c.	242	3	4			
Lighting, Warming, Cleaning, &c...	257	16	6			
Repairs, Alterations, Furniture, &c.	179	5	10			
Meeting Expenses	28	15	8			
Printing, Stationery, Stamps, Telegrams, &c....	221	9	7			
				929	10	11
Officers and Servants:						
Library Staff and Accountant ...	649	10	0			
Gratuity to Mr. Clarke	26	5	0			
House Servants, Cleaners, &c. ...	217	8	8			
Library:—Books and Binding ...	412	1	3			
'Transactions'	467	4	7			
Debentures:						
Three Bonds redeemed	300	0	0			
Interest	988	12	2			
				3061	1	8
Law Charges				49	13	10
Auditors' Fee				10	10	0
Miscellaneous				101	4	1
Balance at Bank and in hand ...				320	19	5
				£4472	19	11

Audited and approved,
TOM MUNDY,
Chartered Accountant.

LIST OF PAPERS.

N.B.—The Council of the Royal Medical and Chirurgical Society deem it proper to state that the Society does not hold itself in any way responsible for the statements, reasonings, or opinions set forth in the various papers which, on grounds of general merit, are thought worthy of being published in the *Transactions*.

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ADDRESS

OF

FREDERICK WILLIAM PAVY, M.D.

LL.D., F.R.S., F.R.C.P.

PRESIDENT,

AT THE

ANNUAL MEETING, MARCH 1ST, 1901

GENTLEMEN,—Of the events that have transpired since the last Presidential Address was delivered, the most noteworthy is the death of our late beloved Queen, who was connected as Patron with our Society. This has been alluded to in the report of the Council, and mention also has been made of the steps taken to give expression to our sympathy and to attest our loyalty and devotion to the Throne. Instituted in 1805, as the words of our Charter state, "for the cultivation and promotion of Physic and Surgery, and the branches of Science connected with them," our Society in 1834 besought and obtained from King William IV, out of his desire to encourage so laudable a design, a Royal Charter of Incorporation "for imparting greater stability and effect to the designs of the said Society," the King furthermore

declaring himself and his successors, if they shall think fit, the Patron of the Society. With the demise of the King his successor was graciously pleased to declare herself our Patron, and under her long and auspicious reign immense strides have been made in the advancement of our knowledge and in the improvement of our art. Those of us who have attained to seniority in the profession can recall a period when upon many points that now stand in a clear light before us, and are to be dealt with in a rational and intelligent way, we possessed no definite knowledge, and thus in relation to them could only bring empiricism to bear. Immeasurable progress in medicine and surgery can truly be said to have been made during the renowned Victorian era that has just been brought to a close. In this progress I think it may fairly be considered that our own Society has contributed its due share of help. By its meetings, by its publications, and significantly by the rich store of literary material contained in its library, to which the active worker is afforded access of the most liberal kind, help may justly be inferred to have been rendered by our Society towards furthering the progress that has been made. I am sure it may safely be affirmed that honest endeavours have been made to promote the efficient carrying out of the objects for which our Society was instituted; and with this expression I am led on to the contemplation of the future, and to say that hopes are to be entertained that sufficient grounds have been given to move the Sovereign, who has just ascended the Throne of his ancestors, to follow their procedure, and graciously think fit to declare himself our Patron.

The modification that has been made in our bye-laws during the year with regard to the publication of papers may be regarded as an eventful one for the Society. We live in times of rapid and great change, and to escape being left behind it is necessary that we should adapt ourselves to the active progress taking place. There is so much now being continuously brought forward to

engage attention that the mind becomes diverted, and interest in a paper is lost by delay in publication. With the conditions now existing, authors desire for their communications speedy and wide publication, and are not content if this is not permitted. Looked at also apart from the author's point of view, diffusion of knowledge is the great object to be attained, and the promotion of this object cannot, it may be considered, do otherwise than produce a beneficial effect. The liberal line of action now in force stands in accord with the course adopted at the Royal Society.

I think I may refer with satisfaction to the meetings which have been held during the year. Material has been brought forward which has drawn large attendances, —indeed, on one occasion our rooms were crowded to an extent that perhaps has not been exceeded before. The great responsibility that is thrown upon the executive has been fully felt, and strenuous endeavours have been exerted to maintain the high reputation which, thanks to the efforts of our predecessors, the Society enjoys.

Before passing to the obituary notices I cannot refrain from alluding to, and acknowledging with appreciation, the courtesy displayed and the assistance rendered by those with whom I have been brought into contact in connection with the distinguished position in which, through your instrumentality, I have been placed. To the Honorary Secretaries I desire particularly to refer. Their office is indeed no sinecure. It is not too much to say that the main stress of work in keeping up the activity of the Society devolves on them. Every one will, I am sure, testify to the great zeal, ability, and efficiency with which the two Honorary Secretaries have during the year discharged their duties; and the retiring Secretary, Mr. Gould, will carry with him our high esteem for the valuable services he has rendered.

The Society has lost by death twenty-one Fellows during the year; they have been taken from us, but they are not allowed to glide unheededly away. In compliance

with time-honoured custom I will now proceed to place before you a sketch drawn from available sources of their lives, so that their memory may be perpetuated in our annals. The order pursued is based upon the date of death.

Dr. William Marcet died at Luxor on March 4th, at the age of 71. He was a scion of a distinguished family. His father was Professor Francis Marcet, of Geneva. His grandfather, Dr. Alexander Marcet, whose wife was the well-known authoress Jane Marcet, was Physician and Lecturer on Chemistry at Guy's Hospital, and was associated with Saunders, Astley Cooper, and others in founding our Society. Young Marcet entered the University of Edinburgh in 1846, and found amongst his fellow-students Charles Murchison, William Overend Priestley, and John Burdon Sanderson. He graduated M.D. in 1850, and coming to London, was appointed Assistant Physician to the Westminster Hospital and the Hospital for Consumption, at Brompton. In 1859 he was elected F.R.C.P., and later became an examiner, and served on the Council of his College.

His chief labours, however, were in the field of physiological chemistry; and his researches gained for him the distinction of F.R.S. as early as 1857. In 1860 he published a book dealing with the effect of alcohol on the human body, especially upon the nervous system. In 1865 he was placed upon the Royal Commission to inquire into the cattle plague, and did yeoman service in the chemistry of the blood and tissues, and the value of disinfectants in that pestilential disease.

Possessed of ample means, he soon relinquished practice, but only to devote himself more closely to scientific research. His earliest work was connected with the action of bile, with the digestion and absorption of fat, and with certain constituents of the intestinal contents. His chief research, however, was connected with respiration, to which he was doubtless drawn by innate love of

mountain life. During his summer vacations in the Alps from 1876 onwards he made numberless researches into the influence of high altitudes upon his own respiration; and during the winters he was constantly at work in the laboratory at University College, which Professor Schäfer kindly placed at his disposal. He thus made many valuable additions to our knowledge of the phenomena of respiration, which were detailed in his Croonian Lectures in 1896. He noted the quantity of carbonic acid expired per minute under various conditions, the quantity of oxygen retained, and the quantity of heat produced by the human body per gramme of oxygen absorbed. His method of procedure was to collect in the summer the air of the Swiss mountains, and that expired by himself at various elevations, and upon these stores to conduct his winter labours.

His good-nature was unbounded, and young workers around him always secured his encouragement. He was President of the Royal Meteorological Society in 1888–9, contributed two papers to our Society, and published other well-known papers and books on climatology and meteorology.

Altogether he was a man of many parts, a patient, persevering, and unostentatious worker, and his investigations threw light upon several physiological points.

Dr. William Chapman Grigg died of enteric fever at Wynberg, South Africa, on March 12th, at the age of sixty. He was the son of the late Rev. S. N. Grigg, for some time rector of Lambley, Nottingham, and was educated at Queen Elizabeth College, Guernsey. He studied for his profession at Birmingham, Bristol, King's College (London), Vienna, and Edinburgh, became M.R.C.S. in 1863, M.D.Edin. in 1870, and M.R.C.P.Lond. in 1872. From 1874 to 1893 he was Assistant Obstetric Physician to the Westminster Hospital, and for a while Joint Lecturer on Forensic Medicine at its medical school. He was also Physician to Queen Charlotte's Lying-in

Hospital, the Victoria Hospital for Children, and St. George's Dispensary, and a member of several London medical societies. He was largely instrumental in founding the British Gynæcological Society, and was one of its early Presidents. He was an official and an active member of the British Medical Association, possessed much energy, and entered with keen interest into social matters. Moreover he was hospitable, genial, and fond of society, and being in a wealthy position could gratify his tastes in these directions.

The circumstances attending his death were pathetic. Having retired from practice he went to South Africa, and patriotically placed his professional services at the disposal of the Medical Department of the Army, travelling in the vessel that conveyed Lord Roberts to the seat of war. His services being accepted he was sent as a voluntary physician to the hospital for enteric cases at the camp at Modder River, where, living in a daily temperature exceeding 100° F. upon food insufficient and indigestible, he soon lost his health, but refused to quit his post. Shortly, however, he was found to be suffering from enteric fever himself, and was taken to Wynberg, where, notwithstanding the skill and careful attention bestowed by several medical *confrères*, he succumbed about ten days after his arrival. In his last letter to friends in England he wrote, "Should you never again hear from me, remember I have sacrificed my life in the cause of my country." He was buried at Wynberg with full military honours, and a memorial service was held at Christ Church, Mayfair, of which church he had been for twenty-five years churchwarden.

Sir William Overend Priestley, M.D., LL.D.Edin., F.R.C.P.Edin. and Lond., M.P., died on April 11th at his residence in Hertford Street, Mayfair, in his seventy-first year, after an illness of about four months' duration caused by a malignant growth in the pancreas. His father, Mr. Joseph Priestley, of Morley Hall, near Leeds,

was a nephew of the celebrated chemist, the discoverer of oxygen. After his early education at Leeds William Priestley proceeded to Edinburgh University, where he soon distinguished himself and gained many prizes. He took the degree of M.D. in 1853, and was awarded the gold medal. As early as 1850 he contributed a paper on "British Carices" to the 'Annals of Natural History,' and in 1851 he published an article on "Pelvic Cellulitis and the Fasciæ of the Pelvis in the Female," which was illustrated with many fine dissections, and was undoubtedly a notable piece of work for anyone only twenty-two years old. At this time began his intimate friendship with Sir James Simpson, to whom he was Physician's Assistant when Simpson's fame was attracting to Edinburgh patients from all parts of the world.

Priestley came to London in 1856, and married in the same year Miss Eliza Chambers, daughter of Robert Chambers, of the celebrated Scottish publishing firm, a lady well known as the authoress of several papers on subjects relating to sanitation. He became F.R.C.P.Edin. in 1858, and was elected in 1864 to the corresponding grade in the London College, in which he subsequently held office as Councillor and Censor. He was President of the Obstetrical Society of London in 1875, and President of the Metropolitan Counties Branch of the British Medical Association in 1895, when the Annual Meeting of the Association was last held in London. He was also on two occasions President of the Section of Obstetrics at annual meetings of the Association, and was an honorary member of several foreign medical, obstetrical, and gynæcological societies.

Priestley's singular charm of manner, his hospitality and amiability, coupled with the fact that he was known to be Simpson's assistant and friend, brought him rapid advancement in the branch of work which he followed. He was appointed Lecturer on Midwifery at the Grosvenor Place School of Medicine and at the Middlesex Hospital, and Physician to the Samaritan Hospital for Women,

and in 1863 he succeeded Dr. Arthur Farre as Professor of Midwifery in King's College and Obstetric Physician to King's College Hospital, to the chagrin of the two Assistant Obstetric Physicians, Drs. Tanner and Meadows, both of whom in consequence resigned. But Priestley's selection was thereafter fully justified by his success as lecturer and clinical teacher, whilst for years he had probably the most fashionable and lucrative obstetric practice in London, and was selected by the Queen to attend the late Princess Alice and the Princess Christian during their accouchements.

Unfortunately in 1864 he had a severe attack of diphtheria, followed by paralysis of many months' standing, during which time Dr. Charles West occupied his place as Lecturer. In 1872, when he was only forty-three years of age, he resigned his appointments at King's College, and devoted his energies to private practice and matters appertaining to questions of social interest. In 1887 he delivered the Lumleian Lectures at the College of Physicians on the "Pathology of Intra-uterine Death." Articles, it may further be said, were contributed by him to Reynolds' 'System of Medicine' and Allbutt and Playfair's 'System of Gynæcology.'

He received the honour of knighthood in 1893, and in 1896 was selected without contest to represent the Universities of Edinburgh and St. Andrews in Parliament. His stay in the House of Commons was too short to permit of any notable achievement; at the same time, however, the Vaccination Act of 1898 bears one enactment which he carried against the Government with whom he usually voted, viz. that the conscientious objector shall have an opportunity of reconsidering the position when his child is five years old. Sir William Priestley proved a capable, sympathetic, prudent, and very useful member, and his opinion came to be highly valued.

The above were the leading facts in Sir William Priestley's life. His character was gracefully summed up directly after his death by a friend of thirty-five

years' standing in the following words:—"One of the kindest and most amiable members of the profession has gone to his rest. He leaves a happy memory behind him. He did his work well, always with thoroughness and a nice sense of honour. Sensitive by nature, he remained guileless, and even under provocation was gentle. He spoke ill of no man, and always followed the things that made for peace. He was the best of friends and companions, sympathetic and true, a capital sportsman, and endowed with a saving grace of humour. How he enjoyed to hear and relate a good story! His influence was always for good, and he advocated, as he always took, the highest line of procedure in practice. We shall long miss our genial and wise friend. The blank his departure must make in his own and many other circles is too sad to contemplate. Let us be thankful we have had him. We can never forget him."

Professor George Viner Ellis died on April 26th at the advanced age of 87, at his birthplace, Minsterworth, Gloucester. His studentship career at University College was attended with prominent success, and ended in his appointment as Demonstrator of Anatomy under Professor Quain. He also studied anatomy during his vacations in Paris and Berlin. He became M.R.C.S. in 1835, and was one of the original 300 Fellows of the College elected in 1843. In 1850 he succeeded Quain as Professor of Anatomy, and held the post for twenty-seven years, when he retired with the title of Emeritus Professor. He scarcely if at all engaged in practice, but devoted his whole working life to the study and expounding of Anatomy, and his 'Demonstrations of Anatomy,' first published in 1840, and of which the eleventh edition appeared exactly fifty years subsequently, was the standard guide during that long period to generations of English-speaking students in the dissecting room. He also edited, in 1856, Quain's 'Elements of Anatomy,' in which the description of the nerves was mainly his own

work; and in 1863 he published two volumes of life-size 'Illustrations of Dissections.'

As a teacher and lecturer he was most conscientious and exact, and his language was precise. Although much distressed when any of his men failed to satisfy the examiners at the College, he was usually too austere and unsympathetic and too strict a disciplinarian to be generally beloved of his students, though he was held in the highest respect by all. That he possessed complete control over his class was proved by the fact that he absolutely banished smoking, to which he had a rooted objection, from his dissecting room.

After his retirement he occupied his time with gardening, and teaching the older boys of his parish in a night school. Probably most of us here present owe much to the masterly and lucid exposition of George Viner Ellis in the department of study to which he devoted himself.

Mr. John Wiblin became a Fellow of this Society in 1852, and practised his profession for more than fifty years in Southampton. He studied medicine at University College, London, and in Paris; became M.R.C.S.Eng. in 1837, and obtained the Fellowship by examination in 1849, and took the Licence of the Royal College of Physicians, Edin., in 1859.

At Southampton he held several responsible posts, viz. that of Medical Inspector of Emigrants, Sanitary Surgeon to the Board of Trade, and Medical Superintendent of Quarantine to the Royal Mail and Union Steam Packet Companies. He died at his residence, Wimborne, on April 27th.

He was the author of a small work, 'The Medical Student's Guide to the Hospitals of Paris,' and contributed a few papers on rare cases to the medical journals, one of which was a successful case of amputation at the shoulder-joint.

John Neville Colley Davies-Colley, M.A., M.B., M.C., F.R.C.S., died on May 6th at his country house, Borough,

Pulborough, Sussex, at the age of 57, from carcinoma of the liver, after an illness of six months' duration borne with exemplary resignation and fortitude.

He was one of the four sons of Dr. Thomas Davies-Colley, formerly senior Physician to the Chester General Infirmary, and received his University education at Trinity College, Cambridge, and his medical training at Guy's Hospital, where he entered as a pupil in 1864. He was a successful student and athlete, and in June, 1868, was appointed Surgical Registrar and Tutor. In that year also he obtained the M.B. and M.C. degrees at Cambridge, and became M.R.C.S.Eng. He advanced to the Fellowship of the College of Surgeons in 1870, and was next appointed Demonstrator of Anatomy at Guy's. In 1872, when a vacancy occurred on the surgical staff by the appointment of Mr. Edward Cock to the position of Consulting Surgeon, and the promotion of Mr. Bryant to the vacant surgeoncy, Mr. Davies-Colley was selected as Assistant Surgeon.

In 1880, upon the resignation of Mr. Cooper Forster, Mr. Davies-Colley became full Surgeon, and retained the post for nearly twenty years, *i. e.* until the end of 1899, when, upon ascertaining the nature of his illness, he resigned his appointments and retired from practice.

During his attachment to Guy's he lectured first on Experimental Philosophy, then on Anatomy, and lastly for several years he gave half the lectures on Surgery. His method of delivery was slow and deliberate, and was adopted by him to overcome a proclivity to stammer with which in early life he had been troubled.

Besides his appointments at Guy's he was elected in July, 1896, a member of the Council of the Royal College of Surgeons, and was successively Surgeon and Consulting Surgeon to the Seamen's Hospital, Greenwich ; Examiner in Anatomy, at the Conjoint Board of the two Royal Colleges, for the Fellowship of the Royal College of Surgeons; and to the University of Cambridge; and lastly, he examined in Surgery for the two Colleges and

for his University. His mode of examining, from his urbanity and the clearness with which he stated his questions, drew forth the appreciation of candidates. By his students generally he was greatly esteemed, as he was clear, painstaking, punctual, courteous, and possessed of a fine memory—qualities which rendered his teaching precise and eminently useful. He had such a keen sense of duty that he would not allow a lucrative country fee to tempt him to omit a lecture to his class. He devoted the chief of his time and energies to the work of his school and hospital, and was so scrupulous in the performance of these duties that he was perhaps less known to the profession generally than many other surgeons of similar standing.

To his colleagues he was most genial, and always ready to give advice in any difficult case or operation; and as his judgment was sound and his experience ripe, his opinion was often sought by the other members of the staff. He was a bold and successful surgeon, and to the last undertook the biggest operations. For many of the foregoing details I am indebted to Mr. Charters Symonds' appreciative sketch of his colleague, from which the following quotation must not be omitted:—"In December Mr. Davies-Colley gave his last lecture before the vacation, visited his wards as usual, and leaving everything in order went for the Christmas holiday, never to return. To most this was a sad surprise, to him it was intention. Seeing the hopelessness of his condition, he at once resigned his various appointments. . . . . His Christian resignation, his heroic submission to the blow which had fallen upon him, when so much remained to be done, will long be remembered by those who had the privilege of visiting him."

Mr. Davies-Colley was not a voluminous writer, but contributed four excellent articles to Heath's 'Dictionary of Surgery,' one to Morris's 'Treatise of Anatomy,' and several records of cases to the medical periodicals. In the 'Transactions' of our Society are three papers of

which he was the author; and all, I believe it is considered, are first-rate exemplifications of practical surgery. For many years he was the surgical editor of the 'Guy's Hospital Reports,' and in almost every year since 1870 papers and reports from his pen have appeared in those pages. He was engaged for years in writing a work on surgery, which, had he lived to complete it, must, in the opinion of one of his surgical colleagues, have taken a foremost position.

With such personal and professional endowments it is not surprising that Mr. Davies-Colley earned for himself the deepest regard of colleagues and students. In testimony of this, allusion may be made to the illuminated address presented to him during the last week of his life, bearing six hundred signatures, and expressing a sense of profound gratitude for his devotion to duty and other sterling qualities, and personal sorrow at his forced resignation of his official posts.

Mr. Davies-Colley married the daughter of the late Mr. Thomas Turner, formerly Treasurer of Guy's Hospital, and was consequently brother-in-law to Dr. F. Charlewood Turner, whose death was recorded by my predecessor in his Presidential Address of 1900.

Dr. Julius Althaus was born in 1833 at Detmold, in Germany, where his father was a minister of the Reformed Church, and died in London on June 11th. He studied at the Universities of Bonn, Göttingen, Heidelberg, and Berlin, at the last of which he obtained the M.D. degree in 1855, and was coetaneously selected to accompany Müller, the physiologist, on a voyage of research in Sicily. He afterwards worked in Paris, where he followed Charcot's practice, and in Vienna, Prague, and London; and finally settling here, he became M.R.C.P. in 1860.

As assistant to the late Dr. R. B. Todd he had opportunities of undertaking the electrical treatment of patients in King's College Hospital. From the first Dr. Althaus devoted himself chiefly to diseases of the nervous system;

and in 1866 founded the Hospital for Epilepsy and Paralysis, Regent's Park. He acted as Physician to the Hospital until 1894, when he was elected its Consulting Physician.

Dr. Althaus published many books and papers upon nervous diseases, particularly upon their electrical treatment. His work on 'Medical Electricity' attained considerable success. Its third edition was published in 1873, and it was translated into French, German, and Italian. Another book, 'The Failure of Brain Power,' which had a large circulation amongst laymen, reached a fifth edition. His views as to electrical treatment apparently did not receive general professional support. Amongst his varied attainments it may be specially mentioned that he was a skilful musician.

His fatal illness began in prolonged attacks of irregular gout, upon which supervened gouty phlebitis followed by gastro-enteritis and inflammation of the peritoneum.

Dr. Benjamin Douglas Howard died on June 21st at the summer residence of his friend Dr. Andrew H. Smith, at Elberon, New Jersey, U.S.A., at the age of 63. He was a native of England, but went to America in his early manhood, and graduated as M.D. of the College of Physicians and Surgeons, New York, in 1858. During a great part of the American Civil War, lasting from 1861 to 1865, he served with distinction in the medical department of the North, becoming eventually Medical Director in the army of the Potomac. Those days were before the Listerian epoch, but Dr. Howard was then treating gunshot wounds of the chest by hermetic sealing rather than drainage, and he attracted considerable attention to himself and his method. He invented, too, an army ambulance waggon, which gained the first prize at the Paris International Exhibition, and which remains to the present day, with certain modifications, a model of its kind.

In 1873 his health failed, and he travelled and studied in Europe, Asia, and Africa. He then resided in London

for a time, became M.R.C.S.Eng. and F.R.C.S.Edin. in 1877, returned to New York to practise, and was appointed Professor of Operative Surgery in the University of that city. He was subsequently Professor of Surgery in the institutions at Long Island, Vermont, and Cincinnati, and finally devoted himself to a widely spread investigation of the state of prisons. With this object he visited the chief prisons of the world, and secured, it is said, the adoption of many reforms.

Daniel John Leech, M.D., D.Sc., F.R.C.P. The death on July 2nd of Professor Leech, at the age of 60 years, called forth a wide-spread and unanimous expression of deep sympathy. He was one of the foremost leaders of medicine in Manchester, and for years had taken a distinguished part in all public movements having for their objects the health, education, and advancement of the community. The disease which proved fatal to him was cancer of the stomach, and for three months he bore his sufferings with exemplary fortitude.

He was the second son of Mr. Thomas Leech, of Urmston, Lancashire, and his elder brother was Sir Bosdin Leech, ex-Lord Mayor of Manchester. He studied at Owens College, Manchester, and qualified as M.R.C.S. and L.S.A. in 1861. In the following year, after a short sojourn in Paris, he became Demonstrator of Anatomy in the Manchester Medical School.

In 1864 he came to London, attended the practice at St. Mary's Hospital, and shortly afterwards embarked in general practice in Manchester. In 1868 he took the degree of M.B.Lond., and was next appointed Honorary Physician to the Hulme Dispensary, and in 1873 Assistant Physician to the Manchester Royal Infirmary. In 1875 he was admitted a member of the Royal College of Physicians, and was elected a Fellow in 1882 after becoming M.D.Lond. in 1876. In 1878 he was appointed Physician to the Manchester Royal Infirmary, which post he held for twenty-one years, viz. until his

resignation in 1899, when he was appointed Consulting Physician. He was also on the staff of the Manchester and Salford Hospital for Skin Diseases, and the Cancer Hospital (both of which he was instrumental in founding), and was Consulting Physician to the Deaf and Dumb Institute in Old Trafford. From 1876 onwards he was firstly Lecturer on and subsequentiy Professor of Materia Medica and Therapeutics in Owens College, and gave his time, energy, and pecuniary support to the perfecting of his lectures and the establishment and maintenance of the fine museum of materia medica that Manchester now possesses, and to the organisation of experimental laboratories in connection with the same branch of medical science. But eminent as were his services to Owens College in his own department, he served it also as member of the Senate and Court of Governors; and after the establishment of the Victoria University became Chairman of Convocation, pro-Vice-Chancellor, and from 1891 representative of the University upon the General Medical Council, for which services the honorary degree of D.Sc. of the University was in 1895 conferred upon him.

In succession to the late Sir Richard Quain, Professor Leech was Chairman of the Committee of the General Medical Council charged with the revision of the British Pharmacopœia, and the edition of 1898 was published under his supervision. He held many posts in the British Medical Association, amongst which were the Presidency of the Lancashire and Cheshire Branch, and of the Therapeutic Committee of the Association. He was a most active member, and for five years President of the Manchester and Salford Sanitary Association, and in that capacity produced several most able reports dealing with the pollution of rivers, the smoke nuisance, the adulteration of milk and other foods, and the housing of the working classes. For five years he was editor of the 'Medical Chronicle,' and he was a constant contributor to its columns. To the Balneological Committee

of our Society he contributed in the last year of his life a valuable report upon the health resorts of North Wales. He was an examiner at the Royal College of Physicians and at the University of London, and at the former institution delivered the Croonian Lectures for 1893 upon the Pharmacological Action and Therapeutic Uses of the Nitrites and Allied Compounds, a subject to which he had given most careful experimental and clinical attention.

It is unnecessary to furnish further instances of the vast work in which Professor Leech was constantly engaged; suffice it to say that his energy and enormous capacity for work were always devoted to objects connected with the public welfare. He was thoughtfully helpful to others, particularly those who were in struggling circumstances, and many, it has been said of him, were the impecunious students who had cause to bless him for generous and timely assistance.

All who knew him were impressed with the gentleness and attractiveness of his nature. He was happy, sanguine, and generous. His uprightness, sincerity, and zeal were conspicuous. He rarely took relaxation, and generally spent his holidays in visiting and studying the various health resorts of Europe, or in attending medical congresses. He was truly a great physician, teacher, and worker. His friend Prof. Dreschfield has written of him that "his name will always occupy a foremost place in the history of the Manchester Medical School, to which he has given the greater part of his life with such singular devotion."

William Charles Storer Bennett, F.R.C.S., L.D.S., L.R.C.P., died quite suddenly of heart disease on July 19th, at the early age of 48. Throughout his life he was a person of delicate health, but by his ability and industry he succeeded in securing many prizes during his studentship at the Middlesex and Dental Hospitals, and afterwards rose to a high position in the dental branch of the profession. Already a past President of the

Odontological Society, he was, at the time of his death, President of the Representative Board of the British Dental Association, and, a month before his death, had been appointed Examiner in Dental Surgery by the Royal College of Surgeons. For a number of years he was Dental Surgeon and Lecturer on Dental Surgery at the Dental Hospital of London, and died whilst filling the same posts at Middlesex Hospital.

He was always fond of teaching, and devoted a large portion of his time to his public duties, even latterly when he had become aware that his hold upon life was precarious.

His end came suddenly in the evening at his country house at Maidenhead, to which he had gone after seeing his patients in London as usual during the day. His funeral, at Brompton cemetery, attracted a large gathering of his professional brethren.

Dr. Robert John Spitta, who died on August 2nd at Clapham, was born at Peckham in 1820, entered King's College in 1836 and St. George's Hospital in 1837, and gained many prizes at both schools. He qualified as L.S.A. in 1841 and M.R.C.S. in 1842, and graduated M.B.Lond. in 1842 and M.D. in 1858. He was Demonstrator of Anatomy in St. George's Medical School in 1842 and 1843. He took considerable interest in analytical chemistry, and was one of the first to make a quantitative analysis of the chief German mineral waters.

He married and settled in Clapham in 1842, his great friend Sir Prescott Hewett being his best man. He practised for forty-five years, retiring in 1887. He contributed a case of cyanosis to the 'Transactions' of our Society in 1846, and served on our Council in 1878–9. He published papers on various subjects, principally on cholera, and his services to the residents of Clapham during epidemics of that disease were recognised by the presentation to him of a valuable piece of plate.

He retained his faculties and interest in his profession until within a few days of his decease, which occurred in the house in which he had resided for fifty-eight years.

Sir William Stokes, M.D., M.Ch., F.R.C.S.I.—The death of Sir William Stokes at the Base Hospital, Pietermaritzburg, Natal, on August 18th, at the age of sixty-one, came as a great shock to his numberless friends, and caused a wide expression of the deepest regret. He had been in South Africa more than five months, serving as Consulting Surgeon to Her Majesty's Forces at Frere Camp, Colenso, and Mooi River. Until the beginning of June he had been in fairly good health, but was then in hospital for a fortnight with cough and jaundice, and went to Durban to recruit. After two weeks' absence he returned to work, and was expecting to come home shortly when his fatal illness began.

Sir William Stokes was the second son of Dr. William Stokes, F.R.S., Regius Professor of Physic in the University of Dublin, famed for his works on "Diseases of the Heart and Lungs." He was a cousin of Sir George Gabriel Stokes, the present Lucasian Professor of Mathematics in the University of Cambridge, past M.P. for the University, and past President of the Royal Society.

He was educated at the Royal School, Armagh, and Trinity College, Dublin, and studied medicine in the School of Physic in Ireland, the Carmichael School of Medicine, and the Meath and Richmond Hospitals, Dublin. He graduated as B.A.Dublin in 1859 and as M.D. and M.Ch. in 1863, and became F.R.C.S.I. in 1873. After his graduation he studied in Berlin, Paris, Vienna, and London. From 1864 to 1868 he was Surgeon to the Meath Hospital, but resigned the post on his appointment to the Surgeoncy of the Home Industry Hospitals. He was elected Professor of Surgery in the Royal College of Surgeons in Ireland in 1872, and held the post up to the end of his life. He also lectured for

a time on Surgery in the Carmichael School of Medicine. He was successively a member of Council and President (1886–7) of the Royal College of Surgeons in Ireland, and it was then that he was knighted. He had examined in Surgery in the Queen's University in Ireland and in the University of Oxford, was Honorary President of the four consecutive International Medical Congresses held respectively at Berlin, Rome, Moscow, and Paris, and ex-President of the Pathological Society of Dublin and of the Irish Graduates' Association. He delivered the Address in Surgery at the jubilee meeting of the British Medical Association at Worcester in 1882, and thereby gained for himself a wide-spread reputation as an orator. In 1888 he was elected Surgeon to the Meath Hospital, and held the post until his death, but severed his connection with the Richmond Hospital. In 1892 he was appointed Surgeon-in-Ordinary to the Queen in Ireland.

He was a prolific writer of papers on clinical and operative surgery in the 'Transactions' of various Societies, and in the medical periodicals. One of his papers on "Supra-condyloid Amputation of the Thigh" appeared in the 'Transactions' of this Society in 1870. He contributed some letters from the "front" to the 'British Medical Journal,' which form a valuable record of his splendid services with the troops. He died in the execution of his duty—a fitting end to his distinguished and useful career.

He was a loyal son of Ireland, who devotedly spent his life in the relief of human suffering. He was an ideal clinical teacher, having the manner, voice, and accuracy suited to the vocation, and it was a delight to hear him speak.

Appreciative notices of their deceased friend have been penned by Sir William Gairdner, Prof. Ogston, and Sir John W. Moore. "Truly," says Prof. Ogston, "he was a man whom it was good to have known, and whose

life was a bright example of all that was great and noble and true."

Sir Henry Wentworth Dyke Acland, Bart., K.C.B., M.D., F.R.C.P., F.R.S., died at his residence, Oxford, on October 16th, at the advanced age of 85, honoured and respected by the many persons in every rank of society to whom he was known. He had for years been in failing health, but his final illness lasted less than a week.

He was descended from a long line of Devonshire squires, records of whom, even in Plantagenet times, still exist; and the family has in its various generations furnished many notable men. Sir Henry's father was Sir Thomas Dyke Acland, the well-known Member of Parliament for the county of Devon. Sir Henry, who was his fourth son, was educated at Harrow and at Christ Church, Oxford, but being of delicate health he was advised in 1838—that is whilst he was yet an undergraduate—to undertake a tour in the Mediterranean. He visited the Levant in H.M.S. Pembroke, and with youthful ardour explored the site of the ancient city of Pergamos. The volume containing his plan and description of the place was published in 1839, and met with much approbation. Returning to Oxford he obtained his B.A. degree in 1840, and was elected a Fellow of All Souls.

He next proceeded to study medicine for three years at St. George's Hospital, London, where Sir Benjamin Brodie was then supreme; and subsequently for one or two years in Edinburgh, where he resided with Dr. Alison. In 1844 his essay on "Feigned Insanity" gained for him the gold medal in Medical Jurisprudence. In 1845 he was appointed to the post of "Lee's Reader in Anatomy" at Oxford, and in 1846 he graduated as M.B. at that University and became L.R.C.P.Lond. In 1847 he was elected Physician to the Radcliffe Infirmary, Oxford, became F.R.S. at the early age of thirty-two, and acted as local Secretary to the British Association for the

Advancement of Science at its second meeting in Oxford. In 1848 he became M.D.Oxon., and in 1850 F.R.C.P. Lond.

Whilst an undergraduate he made two special friendships,—one with Henry Liddell, his tutor, who subsequently became Dean of Christ Church; the other with John Ruskin. These two ties, broken only by death, had a profound effect upon his career. Sir Benjamin Brodie also befriended him and helped him with good counsel throughout his life. Professor Alison, Dr. John Goodsir, and Professor Owen also assisted largely in the development of those aspirations the realisation of which by Dr. Acland gradually changed the whole trend of education at Oxford.

In the forties the stethoscope and microscope were only in their early stage of use in clinical medicine, but Acland extensively availed himself of each of these aids to diagnosis. Oxford had no School of Science when he first lectured on Anatomy. Here was the opportunity, here also the man. He worked assiduously at Comparative Anatomy, went to Shetland for practical work amongst the marine fauna, amassed slides and preparations, and introduced microscopes. His lectures and demonstrations were highly appreciated by undergraduates, but received scant recognition from older members of the University. Shortly he proclaimed the necessity of a museum. Buckland's treasures, Acland's own collection, and Hope's entomological specimens required a worthy habitation. But "the proposal was vehemently denounced, by economists on the ground of cost, by the old-fashioned classicists as intrusive, by theologians as subtly ministering to false doctrine, heresy, and schism." Backed, however, by Daubeny, Dean Liddell, Dr. Pusey, and Professor Phillips, Jacobson, afterwards Bishop of Chester, and Charles Conybeare, Acland pressed on, the money was in time voted, the design adopted, and on June 20th, 1855, the foundation stone of the University Museum laid by Lord Derby. "With it was laid the

oundation of a new era in Oxford, which was to effect a revolution in the old University, and to give hitherto undreamed-of advantages for scientific training to succeeding generations of Oxford men." Obstructive tactics were still pursued by the opposition whilst the Museum was in process of construction, but a noble building was eventually erected. The Museum was so far finished in 1860 as to be fit to receive the annual meeting of the British Association, and in the Library, devoid of books and shelves, took place the famous encounter between Wilberforce, Bishop of Oxford, and Huxley on "Darwinism." Science, however, was not yet cordially welcomed, but was generally regarded as antagonistic to "morals, and religion, and philosophy, and history, and language." But Science had come to stay and to flourish; and whereas in 1840 the teachers of scientific subjects in Oxford were about nine, before Sir Henry Acland's death they had increased to fifty-four.

In 1861 a Microscopical Society was established in Oxford, with Acland as its first President, and the meetings drew large attendances. In planning the Museum, Acland's idea was to found an institution for the investigation and teaching of all that concerns man and his dwelling-place, in health and in disease. Of these several departments, those of physics, physiology, human anatomy, and anthropology have progressed well; but in other departments little advance has been made, or advance, as in the sanitary laboratory, almost entirely at Acland's own expense. In the training of medical students Acland held that the scientific subjects which form the basis of medicine, viz. chemistry, physics, physiology, etc., could be better studied at Oxford, but that purely clinical work could be far better undertaken in London with the resources afforded by its teeming population.

In 1851 Acland was appointed Radcliffe Librarian, and in 1857, upon the death of Dr. Ogle, he became Regius Professor of Medicine. He resigned the latter post in

1894. He served on two Royal Commissions—the Cubic Space Commission in 1867, and the Sanitary Commission in 1869. In 1865 he delivered the Harveian Oration before the Royal College of Physicians. It was the first of these Orations delivered in English instead of in Latin. In 1868 he presided over the British Medical Association at its meeting in Oxford, and contributed a presidential address on "Medicine in Modern Times."

In his long professional career Sir Henry Acland was connected with nearly every institution for the sick or aged in Oxford, and under his fostering care they developed marked improvement. He spent much time and energy in forwarding schemes of preventive medicine, especially in the provision of pure water and efficient drainage for the community in general. He was deeply interested in all that concerned the well-being of humanity, and spoke and wrote on all kinds of subjects concerning the national health, sanitation, nursing, medical missions, scientific and medical education, and other subjects; but made no large contribution to practical medicine or pathology. In collaboration with John Ruskin he wrote a fine work on the "Oxford Museum" in 1859. Between that date and 1893 several editions were published, the final one being sumptuously illustrated. He had at one time a very large medical practice. In 1860 he went to America, in the suite of the Prince of Wales, and on his return was appointed Honorary Physician to His Royal Highness, who entered the University in that year. In 1860 also Acland was elected, with Gladstone and Ruskin, an honorary student of Christ Church.

In 1858, upon the founding of the General Medical Council, he became the representative thereon of the University of Oxford, and was President of the Council from 1874 to 1888. During this long period he used his energies for the benefit of the profession, and laboured for the raising of the standard of medical education. He favoured the admission of women to the profession, and

was early of opinion that India would provide a vast field for their services.

In 1883 he was made a C.B., in 1884 a K.C.B., and in 1890 a baronet. Other honours were showered upon him in the shape of honorary degrees and honorary memberships of medical and philosophical societies in Europe and America.

He married in 1846 Sarah, the daughter of William Cotton, F.R.S. Mrs. Acland was a generous dispenser of hospitality, and a kind, thoughtful hostess; and at her death in 1878 a large sum was subscribed to found, as a memorial of her, the Sarah Acland Home for Nurses, which supplies nurses for private and district cases. When Sir Henry Acland retired from the Regius Professorship in 1894 a sum of £3000 was subscribed for a testimonial to him; this he devoted to the enlargement of the Home for Nurses founded in honour of his wife. Dr. and Mrs. Acland had a family of seven, of whom six were sons. The baronetcy has descended to the eldest of them, Rear-Admiral William Alison Dyke Acland. Another son, Dr. Theodore Dyke Acland, is one of the Fellows of our Society.

In 1888 Sir Henry lost the sight of his left eye from hæmorrhage into the vitreous humour, and in consequence of the acute pain the globe was removed by Mr. Henry Power.

Such is a brief outline of the varied life and labours of Sir Henry Acland; but the sketch yet lacks some reference to his personal characteristics. One of these was the enthusiasm with which he entered into any work—the great interest he took in all his co-labourers who endeavoured to carry out their work loyally and well. He had high ideals of life and its duties, and habitually kept them before himself and held them up to others. His well-balanced mind enabled him to look at a subject in its various aspects before framing his conclusions; but having once made up his mind, he held to his opinion with courage and tenacity.

As a physician he was painstaking, methodical, and cautious. He was interested not only in his patients' diseases, but also in the patients themselves.

His guiding star in life was his simple, earnest Christianity, and his piety softened his whole nature. The wording of his will was characteristic of the man. It concludes with the prayer "that the faithful study of all nature may in Oxford and elsewhere lead men to the knowledge and love of God, to faith and to charity, and to the further prevention and relief of the bodily and mental sufferings of all races of mankind."

Dr. Arthur Jamison died on October 17th at his residence in Lowndes Street, Belgrave Square, at the age of fifty-six. Born in Guernsey, he received his medical education at Glasgow University, where he graduated M.D. and C.M. with honours, and was prizeman in 1865. He soon afterwards entered into active work, and joining Dr. Twyford in practice at St. Helens, Lancashire, remained there from 1866 to 1887.

Whatever Arthur Jamison undertook to do he did thoroughly, and the number of years of arduous practice in a large manufacturing centre, with a rigorous climate, left their mark to some extent upon his constitution.

In 1888 he came to London and settled in Belgravia, where he soon drew to himself a large *clientèle* of patients. His high character, personal charm, and cultured literary tastes, added to a fine presence and sympathetic, kindly manner, endeared him to all with whom he came in contact. He was admitted Member of the Royal College of Physicians, London, in 1889, and joined several metropolitan medical societies.

After several attacks of influenza he developed in 1898 the first signs of chronic nephritis, which led to his going abroad for a few months that winter. The following winter he remained in London with apparently somewhat improved health, but towards the end of last June great muscular weakness combined with rapidity of pulse

compelled him abruptly to cease from work. After a few weeks' rest he was advised to go abroad, and a month later, whilst in Switzerland, was attacked with alarming breathlessness. Reaching home with difficulty, he died three weeks after. He was a man of fine abilities, great kindness of heart, and a high standard of honour, and was ever ready to help another. He married in 1875 Isabel, a daughter of the late Rev. Henry Green, of Knutsford, by whom he was nursed throughout his illness, and he leaves a son and two daughters.

Mr. Arthur Symons Eccles died on October 22nd after a short illness attributed to ptomaïne poisoning, at his residence in Mayfair, at the early age of forty-five. He was the fourth son of Mr. J. H. Eccles, M.R.C.S., of Plymouth, who survives him. He studied at St. Bartholomew's Hospital, and became M.R.C.S.Eng. in 1876.

During the Russo-Turkish war he was one of the surgeons, and finally chief surgeon, of the Stafford House Ambulances. He also entered the Imperial Ottoman Medical Service as surgeon, and for his services received the decoration of the Medjidieh, fourth class. After his return he graduated at Aberdeen as M.B. and C.M. in 1879, and then practised for some years at Bayswater. Believing that massage, to be trustworthy as a therapeutic measure, should be conducted by the medical man, he took up the subject as a speciality. He soon became noted for his treatment of neurasthenia and other diseases by massage, and wrote articles and books dealing with many aspects of the subject.

He was a fellow or member of several societies, and particularly interested himself in the West London Medico-Chirurgical Society, which he served in many capacities, especially those of Secretary and President. During his year in the latter office the journal of the Society, now a prosperous publication, was instituted.

Mr. Eccles was of a kindly, generous disposition, most hospitable, and with a wide circle of friends. He

founded the Cavendish Lodge of Freemasons, and was its first Junior Warden.

Mr. William Anderson, F.R.C.S.Eng., L.R.C.P.Lond., died suddenly on October 27th, aged 57. He had enteric fever some years ago, but afterwards suffered from no particular illness until the last week of his life, when he complained of symptoms of dyspepsia, which, however, he had occasionally experienced before. On the day of his death he had expressed himself as better, and was out driving when he was seized with sudden syncope. He reached home, but rapidly succumbed. The cause of death was rupture of a cord of the mitral valve, without apparently any other diseased condition of the heart or other organs.

Born in London and educated at the City of London School, he first studied art at the Lambeth School of Art, and his interest in the subject proved not only a source of great pleasure to him through life, but also contributed largely to his professional success. His studies were conducted at St. Thomas's Hospital, and he gained several prizes, including the Cheselden medal for surgery in 1867, the year in which he became M.R.C.S. and L.S.A. In 1868 he obtained the licence of the Royal College of Physicians, and in 1869 the Fellowship of the Royal College of Surgeons.

For the next two years he was House Surgeon to the General Infirmary, Derby; but in 1871 was elected Demonstrator of Anatomy and Surgical Registrar at St. Thomas's Hospital. In 1873, having been selected for the post of Director of the Japanese Naval Medical College at Tokio, he proceeded thither with his newly wedded wife. Soon after his arrival he was further appointed Medical Officer to the British Legation. During the following six years he not only worked hard as a teacher, himself lecturing on anatomy, physiology, and surgery, but also collected the splendid specimens of Japanese art subsequently purchased by the nation and

now reposing in the British Museum. His catalogue of this famous collection, written by himself, is now, we are told, a recognised authority on the subject. He also wrote two important works, the 'Pictorial Arts of Japan' and 'Japanese Wood Engraving.' For his services he received from the Emperor of Japan the Order of the Rising Sun. His mastery of the Japanese language was rapid, so that he soon discarded the student who interpreted his lectures orally, and lectured in Japanese. Altogether his life in the Far East had very genial surroundings, and he made a multitude of friends from amongst both Japanese and English. Most of his pupils at Tokio are now leading medical men in Japan, and a silver medal bearing his name and effigy was subscribed for and is now an annual prize at the Naval College.

In 1880, at the invitation of his former colleagues at St. Thomas's Hospital, he returned, and was appointed Assistant Surgeon and Joint Lecturer on Surgery. He became Surgeon in 1891, and lectured upon Anatomy from the time of his appointment until 1898, when he became Joint Lecturer on Surgery. He was also for several years Examiner in Anatomy to the Conjoint Board, and afterwards Examiner in Surgery to the Board and to the University of London.

In 1891 he succeeded Mr. John Marshall as Professor of Anatomy at the Royal Academy of Arts. He was author of the section on the genito-urinary organs in Morris's 'Treatise on Anatomy,' and of articles in Heath's 'Dictionary of Surgery' and Allbutt's 'System of Medicine.' He also edited Heath's 'Practical Anatomy,' and published several articles in the medical periodicals, and others, especially of a critical nature, on 'Art,' elsewhere. His intimate acquaintance with Art was particularly valuable to him in his capacity of Lecturer on Anatomy, both at his Medical School and at the Royal Academy of Arts; and, in illustrating his lectures upon the slate with a few precise and rapid strokes, he displayed

the possession of a happy facility that has seldom been surpassed.

He was one of the founders of the Japan Society, and at the time of his decease was chairman of its council—a post to which he was repeatedly elected. Just two days before the end of his life he presided with his usual urbanity at one of the Society's meetings.

As a surgeon he was bold and ready to adopt new ideas. Moreover his great practical knowledge of anatomy constantly came to his aid. Sir William MacCormac writes of Mr. Anderson, a colleague whose friendship he had enjoyed for thirty years, "He was a retiring, perhaps even a shy man; his artistic temperament revolted against the rough contacts of life, and justice was not sufficiently meted out to his many-sided abilities. Yet he possessed a strong individuality; he was strong of purpose, and his convictions, once arrived at, were steadfastly held. He was a loyal friend and colleague, and an upright, honourable gentleman. The place he occupied amongst us will be very hard to fill."

He was conscientious, thorough, and industrious in all he undertook—highly cultured, though quiet and reserved. He had a gracious manner, and was genial, cordial, and much beloved by all with whom he came in contact.

Dr. John Cockle had attained the patriarchal age of eighty-seven when he died at his residence, West Molesey, on November 14th. As far back as 1835 he became M.R.C.S.Eng., and in 1846 took the degrees of A.M. and M.D. at Aberdeen University. In the following year he took the Fellowship of the Royal College of Surgeons by examination, and was elected a Fellow of the Royal College of Physicians in 1869. Early in his career he became Physician to the Royal Free Hospital, which then, however, had no medical school attached to it. He lectured upon medicine in the Grosvenor School of

Medicine, and was elected Physician to the Margaret Street Infirmary and to the City Dispensary.

He had extensive work in his many public appointments and in private practice, but found time for original study, especially in relation to aneurisms of the arch of the aorta and adjoining vessels. Under his direction a valuable collection of drawings of patients suffering from aneurism at the root of the neck was made for the Royal Free Hospital, and, having come across records of two cases of apparent cure of aneurism of the arch due to obliteration of the left carotid artery, he induced Mr. Heath in 1872 to tie the left carotid in the neck of a patient representing a suitable case. The patient recovered and lived four years, and would probably have survived longer had his employment been less laborious.

Dr. Cockle retired from the Physiciancy to the Royal Free Hospital about ten years ago, but continued to practise in Suffolk Place, Pall Mall, coming up daily from his country house, until increasing deafness a few years ago occasioned his complete retirement from professional work.

Amos Beardsley, M.R.C.S., L.S.A., F.L.S., was the eldest son of William Beardsley, of Shipley, in Derbyshire, and died at an advanced age at Grange-over-Sands, Lancashire, on November 20th.

He was apprenticed to Mr. Norman, surgeon, at Ilkeston, and received his medical training at Guy's and St. Thomas's Hospitals. Obtaining his qualifications in 1844, he was for a time surgeon on board the "Dreadnought" at Greenwich. He then practised at Ilkeston, next at Ulverston, and in 1859 went to Grange-over-Sands, where he subsequently practised until his death.

He had a large and extensive country practice, was Chairman of the Grange Local Board for twelve years, and a member of the Cumberland and Westmoreland Archæological and Antiquarian Society. He was also a

good botanist and geologist, and a Fellow of the Linnean and Geological Societies.

His anecdotes and experiences were highly interesting, and would possibly, if collected and published, have equalled, if they had not eclipsed, those in Warren's 'Diary of a Late Physician.' His medical library alone exceeded 2000 volumes.

He was the author of several papers in the medical journals and of two small works.

John Chalmers Brown, M.B., C.M.Edin., who died on December 24th at the early age of thirty-three, was born in Leith, of educated though comparatively poor parents, who strove to furnish the members of their large family with a good education, and thus render them worthy and useful citizens of the state. He was educated at Moray House Free Church School, Edinburgh, and at the University of that city, and early adopted medicine as his career. He graduated M.B., C.M. in 1892, and was immediately appointed House Surgeon and subsequently House Physician to the Leith Hospital. His work at that institution gained for him considerable distinction, and the female students of the Edinburgh Medical School, whom it was his duty to teach, headed by Miss Margaret Todd, the author of 'Mona Maclean, Medical Student,' presented him with an address and a case of instruments in token of their appreciation of his services.

In 1894 he came to London. He first acted as "*locum tenens*" for a few months, and then purchased the nucleus of a practice near Manchester Square. Though he was without friends or influence, and had but small means, his enthusiasm, tact, and skill rapidly brought him success. His kindness of heart and unselfishness attracted to him many friends, and in 1897 he removed to Welbeck Street, but his physical strength subsequently broke down, and he died, as already stated, on December 24th.

Mr. Bowater John Vernon, F.R.C.S., L.R.C.P., was born in 1837, and died somewhat suddenly on January

28th, 1901, having seen his hospital patients as recently as on January 19th. Next day he had a cardiac seizure, accompanied by severe dyspnœa, and the third occurrence of a like attack eight days after proved fatal. At school he had been an athlete, excelling in jumping and running. For many years of late, however, he had suffered from rheumatic trouble, which chiefly affected his wrists and fingers, though fortunately it did not appear to interfere with his skill in operative procedures.

His father was the late Rev. Henry Vernon, for forty years Vicar of Westfield, Sussex. Bowater Vernon received his early education at Marlborough College, and entered the profession as a pupil of Mr. Jowers at the Sussex County Hospital, Brighton. After three years he proceeded to St. Bartholomew's Hospital, where, in 1862, he was House Surgeon to Mr. Wormald, and in 1863 to Sir James, then Mr. Paget. He became M.R.C.S. in 1862, and F.R.C.S. in 1864, and was then appointed Demonstrator of Anatomy in St. Bartholomew's Medical School, retaining the post for several years. He also worked at Moorfields, and filled the posts of Clinical Assistant, and of Curator of the Museum and Pathologist on the retirement of Mr. Bader.

An ophthalmic department being organised at St. Bartholomew's Hospital, Mr. Henry Power and Mr. Vernon were in 1870 appointed Surgeons thereto. Mr. Vernon was also for a time Ophthalmic Surgeon to the Great Northern Hospital, and during twenty-seven years held a similar post at the West London Hospital, acting as Secretary to the Staff through a large portion of that time.

The chief work, however, to which he devoted his life was the teaching of ophthalmic surgery to the students of St. Bartholomew's Hospital. In this he was highly successful. He was regular in his attendance, orderly and methodical in all his work, had great kindness of heart, was gentle and courteous to all, fully alive to the difficulties of the beginner, and helpful and encouraging

to all his class. He was a good observer and had great clinical experience, so that his opinion on a difficult case was very valuable. His operations were well considered beforehand and dexterously performed.

He contributed several years ago some articles to 'St. Bartholomew's Hospital Reports,' and also supplied reports on ophthalmology to the 'Medical Record.' He wrote with clearness and forcibly, but reserved his energies chiefly for teaching.

Dr. Leslie Ogilvie was born at Glasgow in 1853, and died on February 2nd of acute pneumonia, after six days' illness. Educated at the High School, Glasgow, and the University of Edinburgh, he graduated B.Sc. and M.B. in 1876. He was at that time especially interested in geology, of which science Mr. (now Sir Archibald) Geikie was professor, and in anatomy, himself dissecting a shark to illustrate Professor (now Sir William) Turner's monograph on Elasmobranchian fishes.

He studied for a short time in Paris, but returned to Perth to act as *locum tenens*, and was next, for two years, abroad in Paris, Vienna, and elsewhere. He thus acquired a linguistic acquaintance with French, German, and Italian. He commenced practice in London in 1879, and soon became attached to the Bell Street Dispensary, soon afterwards expanded into the Children's Hospital, Paddington Green; and forthwith gave his time and energy to his work at that institution, of which he was at the time of his death the Senior Physician.

He was also during the later years of his life very greatly interested in insurance work. A paper by him which he read before the Actuarial Societies of Edinburgh and Dublin in 1897, on "Some Medical Aspects of Life Insurance," attracted considerable attention. In estimating chances of longevity he opposed the basing of such prospects on statistics, relying rather on the personal appearance, habits, and environments of the proposer

than on his family history. He became M.R.C.P. in 1889, and a member of the Athenæum Club in 1899.

For fifteen years he was Secretary of the Edinburgh University Club of London, and for two years Vice-President and President of the Burns Club. In the latter capacity he discoursed eloquently upon Robert Burns, whose simplicity, humanity, sympathy, and transparent honesty—qualities which were characteristic of himself—he greatly admired.

He had a large circle of friends, attracted to him by his charm of manner and of conversation, his high literary ability, his love of poetry and music, want of affectation, and his general kindness of heart and geniality.

For several years he was an enthusiastic member of the "London Scottish" regiment of volunteers, and an energetic golfer. He has left a widow and three young children to mourn his loss. A brother, Dr. George Ogilvie, is one of the Fellows of our Society.

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WIND EXPOSURE AND PHTHISIS

BY

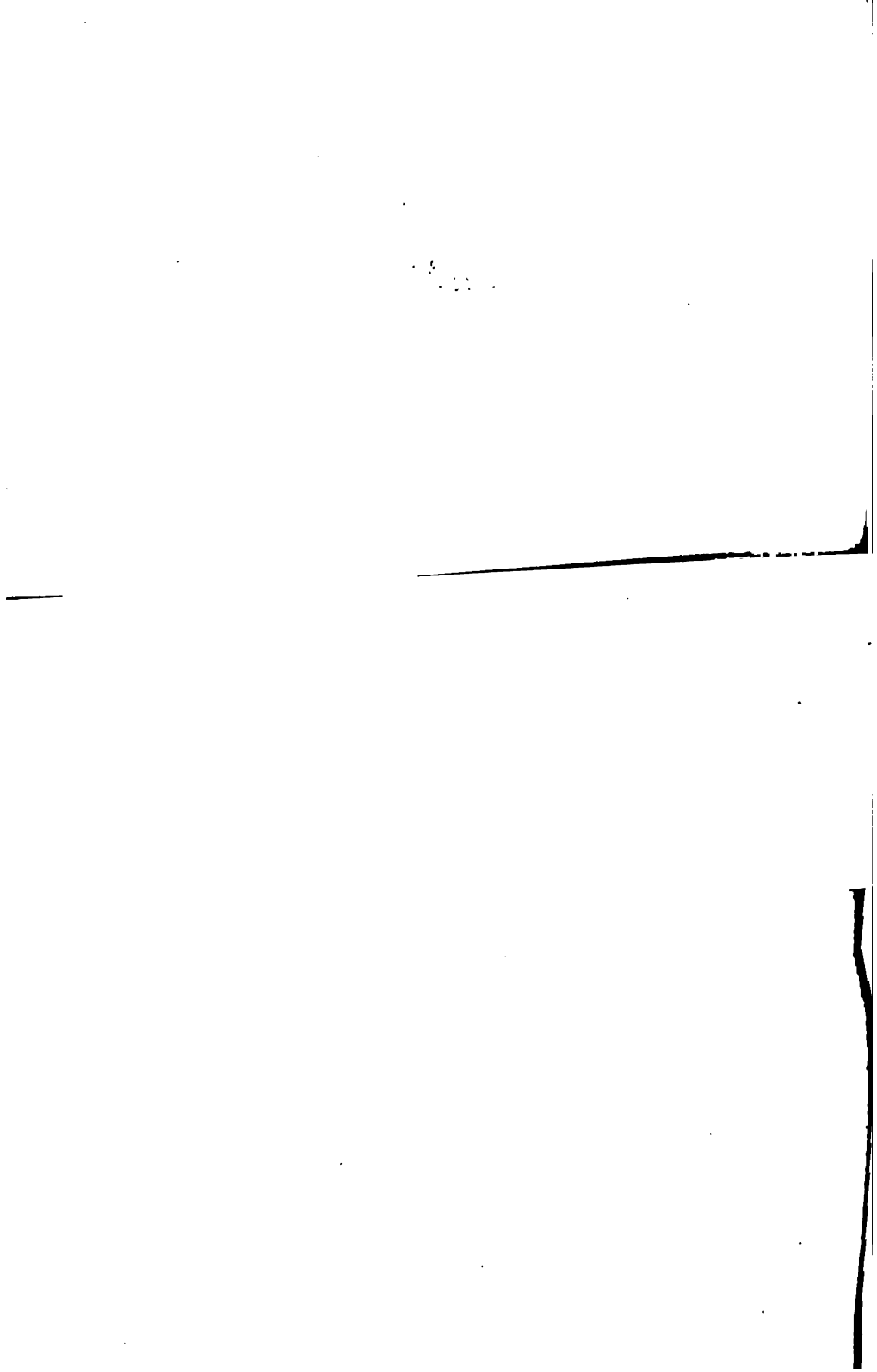
W. GORDON, M.D., M.R.C.P.

NOTE

As many of the maps illustrating my paper on "Wind Exposure and Phthisis" were practically mere duplicates of the tables of figures, it has been considered unnecessary to reproduce more than six of them. These have not been numbered, but are described by titles.—W. G.

are still imperfectly appreciated, and that something still remains to be said, not perhaps on the score of local shelters, but *on the choice of sufficiently wind-protected localities, where the patient's whole time can be spent in a tranquil atmosphere.* I have, therefore, ventured to bring before the Society some facts which made a strong impression on my mind, when studying the distribution of the phthisis death rate in Devonshire.

When the erection of a sanatorium near Exeter was discussed last autumn, I set to work to acquaint myself with the distribution of the phthisis death rate in the Exeter neighbourhood, and in Devonshire generally. From the



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WIND EXPOSURE AND PHTHISIS

BY

W. GORDON, M.D., M.R.C.P.

Received June 27th—Read October 23rd, 1900.

At a time when there seems to be a near prospect of the erection of phthisis sanatoria in various parts of this country it may not be thought inopportune to discuss a subject which bears upon our choice of localities. The relation of wind exposure to phthisis is not a new subject, and wind shelters of some sort are part of the equipment of most sanatoria. But I am strongly of opinion that the facts which Dr. Haviland has placed before the profession are still imperfectly appreciated, and that something still remains to be said, not perhaps on the score of local shelters, but *on the choice of sufficiently wind-protected localities, where the patient's whole time can be spent in a tranquil atmosphere.* I have, therefore, ventured to bring before the Society some facts which made a strong impression on my mind, when studying the distribution of the phthisis death rate in Devonshire.

When the erection of a sanatorium near Exeter was discussed last autumn, I set to work to acquaint myself with the distribution of the phthisis death rate in the Exeter neighbourhood, and in Devonshire generally. From the

annual returns made to the County Council since 1891, I took the annual death rates from phthisis in the rural sanitary districts, and from these I calculated the average annual phthisis death rate in each district.

The first map and Table I illustrate the differences.

The rural districts were chosen, partly because many urban districts have long been phthisis health resorts, and some imported cases have naturally been included in the returns, partly because I thought that the conditions of life in the rural districts would be more uniform than in the urban. The map was by no means what I expected to find it, and it seemed desirable to seek an explanation of its peculiarities.

Relation to general death rate seemed the first point to determine, taking general death rate as a guide to general conditions of sanitation, conditions which have done so much in recent years to modify phthisis mortality.

This second map illustrates the differences in the general death rates of the rural sanitary districts.

From a comparison of these maps it can be seen that phthisis death rate and general death rate have a different distribution. But the inclusion of phthisis in the general death rate tends to mask the actual difference. So a third map was constructed to show the distribution of the general death rates when phthisis had been excluded from them (see Table II). Phthisis death rate and general death rate thus illustrated evidently have a distinctly different distribution.

Further the variations in phthisis mortality from district to district are relatively much greater than those of general mortality. Tavistock has a phthisis death rate more than twice that of Axminster, whilst the extremes of general death rate are only about fourteen and sixteen.

Lastly the year to year curve of phthisis death rate is by no means necessarily the same as the year to year curve of general death rate in the same district. In some districts one curve is actually rising when the other curve is falling.

These considerations leave no room for doubt that, so far

as we can judge from consideration of general death rate, the distribution of phthisis death rate in the rural sanitary districts of Devon is due to some other cause than that of general sanitation.

Relation to rainfall is sometimes laid stress on by writers on health resorts for phthisis, and the rainfall of Devon is notably unequal. It therefore seemed desirable to compare the distribution of the phthisis death rate, with the distribution of the rainfall. Anyone who has tried to make a reliable rain map understands the difficulties of doing so. Not only does rainfall vary in amount from year to year, but to a certain extent its distribution varies also. Stations are often far apart, and neither instruments nor observers are uniformly accurate.

This rain map of Devon can only be regarded as approximate. The figures were taken partly from Symons's 'British Rainfall' for 1897, corrected to the average of 1880 to 1889, partly from Dr. Shapter's 'Climate of South Devon,' which gave practically identical figures for the same places.

A comparison of the phthisis map and the rain map suggests a kind of rough correspondence. Tavistock with the highest phthisis death rate has the most rain, and Axminster with the lowest phthisis death rate seems to have the least rain. However, the correspondence is by no means complete. Crediton with the second highest death rate seems to have a moderate rainfall, and Barnstaple with a considerable rainfall has the second lowest death rate. It therefore occurs to one that instead of rainfall causing phthisis, the two may have a cause in common. If it can be shown that the winds which bring the rain cause an increase in phthisis, the partial correspondence in the maps may be very well explained. In that case we should expect that the heavy rainfall which is deposited on exposed heights would be carried by the wind over sheltered areas beyond, and that on these sheltered areas the correspondence between rain and phthisis would at once come to an end. Take such a district as Newton Abbot Rural on the

sheltered side of Dartmoor. Map V shows the approximate distribution of its rainfall, tinted in proportion. Map VI, also tinted in proportion, shows the distribution of the phthisis death rate in the parishes. From these we see that in Newton Abbot district the parishes with most phthisis, (Ashburton excepted,) have least rain and *vice versâ*. That is to say, the relation between rainfall and phthisis is here the reverse of what obtains in the larger map. We thus see that the rain which, falling on Dartmoor, seems in the map of Devon to be responsible for the heavy mortality of the exposed district of Tavistock, is really carried on to the sheltered district of Newton, and there seems to have nothing whatever to do with phthisis mortality. We can only explain such a contradiction by assuming that, not the rain, but the wind which brings the rain, is the real factor in determining the death rate. I therefore concluded that the distribution of phthisis mortality could not be explained by the distribution of the rainfall. It will, moreover, be remembered that the rainfall in the Black Forest, where Nordrach is situated, is nearly, if not quite, as heavy as the rainfall on Dartmoor.

The relation of soil to phthisis mortality was elaborately discussed in 1867 by Sir George Buchanan, and the conclusions which he arrived at have withstood the criticism which has been brought against them. This geological map gives a general idea of the prevailing rocks of Devon. The west is occupied by a great square of carbonaceous shale which forms on the surface a stiff retentive clay. This square is broken at the south by the impermeable granite of Dartmoor. North and south the shale and granite are bounded by extensive masses of "Devonian" rock, which, although including small areas of sandstone, are composed in the main of limestone and shale and may be generally regarded as retentive. Sandstones, greensand, gravels, and light marls form a permeable triangle in the east of the county.

Such a map indicates that on pervious soils in Devon there is, on the whole, less phthisis, but that the variations in the phthisis rate on the impervious soil are very great.

indeed. The districts, however, are too large, and the general map too lacking in detail, to form a basis for positive conclusions. When we come presently to discuss an individual rural district we can use more detailed geology and smaller units of area, and thus judge more exactly of the part played by soil. But it seems likely that soil alone will not account in Devon for the differences of phthisis death rate.

The relation of wind to phthisis mortality was part of Dr. Haviland's work on the geographical distribution of disease published in 1868. He then enunciated the view that exposure to prevailing winds produces increase of phthisis mortality, and it seems somewhat surprising that his writings have drawn so little general attention. In adopting his method of showing the relation by maps the following modifications appeared desirable:

1. There was no sufficient reason in Devon for separating the mortality of the sexes.
2. The mortality could be better illustrated by proportionately tinted maps in one colour, (a second colour being only used to indicate absence of any deaths from phthisis).
3. The units of area might with advantage be smaller, to allow of more careful comparison with natural features.
4. The influence of general sanitation, rainfall, and soil might well be discussed at the same time.

Consider this map illustrating the wind exposures of Devon, and compare it with the phthisis map.

If the *north* wind were injurious we could not account for the low mortality of the whole north coast. It is, no doubt, a precipitous coast, and such a coast protects the country behind it; but much of the population is distributed in valleys opening seaward, with no cliffs to protect them. The same reasoning applies to *north-west* wind. Moreover, it is evident that the north-west wind has free access to the valleys of the northern rivers, whose course carries them through areas of low phthisis mortality.

If the *north-east* wind exercised a very injurious effect it

would almost reverse the actual distribution of the death rate.

The *east* wind has access to a great part of the low mortality area, although it will be observed that the three areas of lowest mortality are exempt from it.

The *south-east* wind has fair access to all the areas of low mortality.

The *south* wind has access to all the areas of low mortality except, perhaps, Torrington.

We are, therefore, left with the *west* and *south-west* winds only. Can any connection be shown between exposure to these and death rate from phthisis?

Tavistock, on the steep west slope of Dartmoor, is more exposed to west and south-west than any other district, and shows the maximum phthisis mortality.

Crediton, sheltered indeed from the south-west except where the ground rises on the north, is a saddle, across which the west wind blows with unbroken force, and Crediton stands second highest in the list of phthisis death rates.

South Molton by position, slope, and configuration invites both west and south-west winds, and comes third as regards phthisis.

Kingsbridge and *Plympton* are evidently open to both winds, and come next in phthisis.

Okehampton is only partly exposed, and has a more moderate phthisis death rate.

Holsworthy the same, and all Cornwall shelters Holsworthy on the south-west.

Totnes is more sheltered than exposed, and the phthisis death rate is still lower.

Tiverton, perhaps, is rather difficult to judge of. It is more protected from the west, and Dartmoor has broken for it the force of the south-west wind.

Newton Abbot and *St. Thomas* are more protected than any of the foregoing, and their phthisis death rate is less.

Bideford, almost bare of dwellings on its higher lands, and having its population sheltered under its northern

cliffs and in its eastern hollows, is thus self-sheltering, and has a low phthisis mortality.

Honiton, with its complex valley system, is rather hard to judge of. But for Honiton both west and south-west winds have had their violence broken.

Barnstaple seems at first sight a difficulty. But the small valleys running into the folds of Exmoor shelter a considerable proportion of the population from the west wind, and the south-west wind only reaches Barnstaple over the whole length of Cornwall.

Axminster, with the lowest death rate from phthisis, has a most wind-protected formation, with the rather narrow sea opening of its main valley and the numerous side valleys running westward.

On the whole I think it may be said to be probable that in Devon exposure to west and south-west winds increases mortality from phthisis. It is also interesting to note how the population has avoided these winds. The villages of to-day and the hut circles of primitive ages alike are placed where west and south-west gales can least easily reach them. And the Tors of Dartmoor, smooth and rounded on the east and north-east, weathered and jagged on the west and south-west, seem to attest the need for the precaution.

Units of area, however, so large as rural sanitary districts have three disadvantages:

a. They are too large to allow of careful comparison with natural features. The same district often includes very exposed and very sheltered situations.

b. They are too large to allow of careful comparison with geological formation. The same district often includes very permeable and very impermeable soils.

c. They render it difficult to show, (on the small scale necessary,) the distribution of villages and farms, which is indispensable to the consideration of shelter and exposure to the wind; for although the men may be at work in the fields, the women are at home and the children at school,

and for men, women, and children alike, part of the day is spent in the dwelling.

To test, therefore, the accuracy of the impression created by the maps of the county, I mapped out in parishes the district of St. Thomas, and, as the record of phthisis death rate in its parishes was only available for a short period, (two years and four months), I mapped out also the neighbouring district of Newton, where the parish death rates were available for fifteen years, as well as the district of Okehampton, about the centre of the county, and the district of Barnstaple, in its extreme north. In these two last I constructed maps of parish phthisis-mortality from ten years' records.

But there is one source of fallacy connected with parishes. The populations in some cases are exceedingly small. It is better to bear this source of fallacy in mind, though I think, in the aggregate results, that it will not mislead us.

Consider first the relation of wind exposure to phthisis.

This map shows the distribution of phthisis death rate in the parish of St. Thomas; (for figures see Table III). That one shows the heights and hollows, villages, and farms.

A short survey, I think, suffices to suggest that exposure to west and south-west winds may have a connection with the phthisis death rate. To make certain of this let us divide the parishes into the following three groups:

Group I.—Parishes where the dwellings are well sheltered from west and south-west winds.

Group II.—Parishes where the dwellings are fully exposed to west or south-west wind or to both.

Group III.—Parishes where the dwellings are imperfectly sheltered from these winds.

Compare the collective mortality from phthisis in these groups. The results are as follows:

Group I, (sheltered), contains nine parishes with a collective population of 3850, having an annual phthisis death rate of ·24 per 1000.

Group II, (exposed), contains eighteen parishes with a

collective population of 12,732, having an annual phthisis death rate of 1·34 per 1000.

Group III, (imperfectly sheltered), containing seventeen parishes with a population of 10,666, has an annual phthisis death rate of ·57 per 1000.

Thus in St. Thomas district the death rate from phthisis in the exposed parishes is five and a half times greater than in the sheltered parishes, and nearly two and a half times greater than in the imperfectly sheltered parishes.

These appear very striking figures, even whilst we remember that we are only dealing with a twenty-eight months' record.

Maps VI and VI A are the corresponding maps for the Newton Abbot district, (for the figures see Tables IV and IV A). Here, again, we can trace a connection between the west and south-west winds and the phthisis mortality, but not so remarkably as in St. Thomas. Let us divide the parishes of this district also into three groups and compare them in the same way. We then find that Group I, (sheltered), consists of five parishes, with an aggregate population of 4130, and an annual phthisis death rate of ·83 per 1000.

Group II, (exposed), consists of seven parishes, with a total population of 9148, having an annual phthisis death rate of 1·38 per 1000.

Group III, (imperfectly sheltered), consists of seventeen parishes, containing 11,259 inhabitants, whose phthisis death rate annually is 1·08 per 1000. Thus in Newton Abbot district the death rate from phthisis in the exposed parishes is more than half as much again as in the sheltered parishes, and the imperfectly sheltered parishes show an intermediate mortality.

The figures in this district are not so remarkable, but they are unmistakable.

In the Okehampton district the parishes give the following figures, (Tables V and V A):

Group I, (sheltered), consists of seven parishes, with a

total population of 3400, and an average annual phthisis death rate of ·61 per 1000.

Group II, (exposed), consists of eleven parishes, with a total population of 6250, and an average annual phthisis death rate of 1·72 per 1000.

Group III, (imperfectly sheltered), consists of ten parishes with a total population of 4735, and an average annual phthisis mortality of 1·28 per 1000.

Here the phthisis death rate in the parishes exposed to west and south-west winds is nearly three times as great as in the sheltered parishes, whilst the death rate in the imperfectly sheltered parishes is nearly the mean of those in the sheltered and the exposed.

In the Barnstaple district exactly the same relations obtain, (Tables VI and VI A):

Group I, (sheltered), consists of ten parishes, with a total population of 3806, and an average annual phthisis death rate of ·44 per 1000.

Group II, (exposed), consists of fourteen parishes, with a total population of 7565, and an average annual phthisis death rate of 1·1 per 1000.

Group III, (imperfectly sheltered), consists of twelve parishes, with a total population of 7668, and an average annual phthisis death rate of ·75 per 1000.

Here, again, the phthisis death rate in the parishes exposed to west and south-west winds is nearly three times as great as in the sheltered parishes, whilst the death rate in the imperfectly sheltered parishes is nearly the mean of the other two.

These results are surely very striking.

Therefore the impression derived from an examination of the rural district map of Devon is confirmed by a study of the parishes of these four districts.

We have still, however, to consider the relation of soil to phthisis death rate. (Rainfall in Barnstaple and Okehampton appears to be highest over some of the areas of least phthisis mortality and may be therefore neglected. Rainfall in St. Thomas is practically uniform.)

This map shows the general arrangement of soil in the district of St. Thomas; purple and grey are impervious, the other colours pervious, in greater or less degree. Compare it with the St. Thomas phthisis map; it would seem as if the phthisis mortality were actually higher on the pervious than on the impervious areas, and, as a matter of fact, this is really the case. In other words the presence of wind exposure overshadows any possible influence of soil.

Again, this geological map shows the general arrangement of soil in the district of Newton, and on comparing it with Map VI the influence of soil is by no means obvious. In fact, pervious and impervious soils work out very nearly the same as regards the phthisis mortality upon them.

But if, instead of comparing generally in each district pervious with impervious, we compare pervious sheltered with impervious sheltered only, and pervious exposed with impervious exposed only, we arrive at a very different result. For this purpose I have constructed, (from the inch to the mile geological survey maps), a detailed analysis of the soil of each parish in the districts of St. Thomas and Newton Abbot, (Table VII). From this we may form the groups for comparison, selecting only such parishes as may fairly be considered permeable or impermeable where dwellings are distributed.

[The whole of Okehampton district is practically on impervious soil; the southern half of Barnstaple district is on carboniferous shale, the northern half on Devonian, and a comparison of these two would be difficult, as Devonian itself consists largely of shale.]

In the district of Newton Abbot there are no sheltered parishes with pervious soils, so we cannot draw that comparison, and as the two only exposed pervious soils are situated close to the river on sand and gravel it would be merely misleading to compare them with the impervious exposed; so, as regards the influence of soil, we have only the district of St. Thomas to rely on.

In the district of St. Thomas the annual rate of phthisis

mortality in *sheltered parishes* is as follows: on pervious soil, four parishes, with a total population of 1800, no deaths. On impervious soil, five parishes, with a total population of 2050, ·41 per 1000.

In *exposed parishes*, on pervious soil, seventeen parishes, with a total population of 12,152, 1·32 per 1000.

On impervious soil, one parish, with a population of 580, 1·47 per 1000.

Thus in St. Thomas district we find that soil seems to exercise an influence on phthisis mortality if the influence if wind exposure is removed; but that whatever influence so exerted by soil seems subordinate to the influence of wind exposure.

I do not think that in any of these districts differences in temperature, sunshine, or purity of air can account for the differences in phthisis death rate. Unfortunately, there are no means of scientifically measuring them. But there are no influences which can much affect atmospheric purity; sunshine in St. Thomas, at all events, is pretty evenly distributed; temperature is, no doubt, rather less on the higher ground and on impervious soil, but its differences cannot be great from parish to parish.

It seems, therefore, impossible to escape from the conclusion that for the districts of St. Thomas, Newton Abbot, Okehampton, and Barnstaple, and probably for Devonshire generally, the paramount influence which now determines a higher or lower rate of phthisis mortality is the degree of exposure to or shelter from the west and south-west winds.

My best thanks are due to Mr. Dallas, Curator of the Albert Memorial Museum in Exeter, Dr. Farrant, of St. Thomas, Dr. Harper, of Barnstaple, Dr. Harvey, of Newton Abbot, Mr. Michelmore, Clerk to the Devon County Council, Dr. Slade-King, of Ilfracombe, and Dr. Young, of Okehampton, for the great help they have so very kindly given me.

TABLE I.—*Devon rural districts. Phthisis death rates.*

(Calculated from County Council Reports.)

Name of district.	1891.	1892.	1893.	1894.	1895.	1896.	1897.	1898.	Per 1000 per annum. Average.
Axminster (7 years)	—	1·0	·92	·85	·27	·72	·71	·24	·67
Barnstaple	·84	·74	·74	·81	·73	·97	·63	1·17	·83
Great Torrington	1·56	1·12	·57	1·07	·39	·49	·58	1·37	·89
St. Thomas (2 years)	—	—	—	—	—	—	·92	·90	·91
Honiton	·2	·31	·72	1·56	1·16	1·06	1·06	1·35	·93
Bideford (7 years)	—	·97	·82	·82	·71	1·21	1·09	·90	·93
Newton Abbot	1·38	·72	1·37	1·12	·64	·84	1·19	·64	·99
Tiverton (6 years)	—	—	1·13	1·00	1·12	1·22	·42	1·39	1·05
Totnes (7 years)	—	1·35	1·35	·83	1·18	·60	·66	1·55	1·07
Holsworthy	1·00	1·44	·90	1·22	1·22	1·22	·89	·68	1·08
Okehampton (7 years)	—	1·28	1·64	1·64	·76	1·18	·62	·97	1·15
Plympton	1·36	1·27	1·22	1·09	1·29	1·56	·86	1·18	1·23
Kingsbridge	·90	1·55	1·88	·98	·67	1·28	1·89	·92	1·26
South Molton	1·46	1·38	1·38	1·02	·97	1·41	1·50	1·15	1·28
Crediton	1·86	1·00	1·09	1·38	1·46	1·40	1·02	1·57	1·35
Tavistock	1·95	1·57	1·28	1·74	1·48	·91	·95	1·90	1·47

TABLE II.—*Devon rural districts. Death rate per* 1000 *per annum from all causes* except phthisis.

(Calculated from County Council Reports.)

	Average of			
St. Thomas	2	years	...	12·84
Tiverton	6	„	...	13·45
South Molton	8	„	...	13·51
Honiton	8	„	...	13·59
Newton Abbot	8	„	...	13·66
Bideford	7	„	...	13·69
Totnes	7	„	...	13·84
Kingsbridge	8	„	...	13·97
Great Torrington	8	„	...	14·04
Barnstaple	8	„	...	14·05
Okehampton	7	„	...	14·08
Crediton	8	„	...	14·23
Plympton	8	„	...	14·49
Tavistock	8	„	...	14·59
Axminster	7	„	...	14·63
Holsworthy	8	„	...	14·68

TABLE III.—*St. Thomas District. Influence of shelter from W. and S.W. winds and of soil.*

Name of parish.	Estimated population 1900.	Phthisis deaths in 2½ years.	Phthisis death rate per 1000 per annum.		
			All soils.	Pervious.	Impervious.
I. SHELTERED PARISHES (9), *i. e.* where the *dwellings* are sheltered from W. and S.W.:					
A. *On pervious soils*					
Kenn	827	0			
Ashcombe	167	0			
Mamhead	158	0			
Ide	648	0			
	1,800	0			
B. *On impervious soils*					
Dunsford	665	0			
Bridford	429	1			
Christow	567	1			
Doddiscombsleigh	250	0			
Dunchideock	139	0			
	2,050	2			
	3,850	2	·24	Nil.	·41
II. EXPOSED PARISHES (18), *i.e.* where the *dwellings* are fully exposed *to W. or S.W., or both*:					
A. *On pervious soils*					
Stoke Canon	363	1			
Huxham	111	1			
Topsham	2,833	10			
Pinhoe	761	0			
Sowton	450	0			
St. Mary's Clyst	197	0			
St. George's Clyst	291	0			
Woodbury	1,664	7			
Lympstone	1,097	3			
Whimple	656	2			
Aylesbeare	784	3			
Rockbeare	451	1			
Farringdon	215	1			
Otterton	725	4			
E. Budleigh	866	1			
Bicton	121	1			
Colaton Raleigh	567	3			
	12,152	38			
B. *On impervious soil*					
Tedburn St. Mary	580	2			
	12,732	40	1·34	1·32	1·47

TABLE III—*continued.*

Name of parish.	Estimated population. 1900.	Phthisis deaths in 2½ years.	Phthisis death rate per 1000 per annum		
			All soils.	Pervious.	Impervious.
III. IMPERFECTLY SHELTERED PARISHES (17), *i.e.* where the *dwellings* are partly sheltered partly exposed as regards W. and S.W.:					
Whitstone . .	494	0			
Holcombe Burnell .	203	0			
Alphington . .	1,064	1			
Shillingford . .	66	0			
Exminster . .	2,337	3			
Powderham . .	203	0			
Clyst Hydon . .	298	1			
Clyst St. Lawrence	126	0			
Broadclyst . .	2,003	2			
Honiton Clyst .	274	1			
Rewe . . .	247	0			
Netherexe . .	70	0			
Upton Pyne . .	460	1			
Poltimore . .	361	0			
Brampford Speke .	350	0			
Ashton . . .	209	1			
Kenton . . .	1,901	4			
	10,666	14	·57	*	*

* (As the degrees of exposure differ, the soils have not been compared here.)

TABLE IV.—*Newton Abbot Rural District (Influence of shelter from W. and S.W. winds).*

Name of parish.	Estimated population 1898.	Phthisis deaths in 15 years.	Phthisis death rate per 1000 per annum.
I. SHELTERED PARISHES (5):			
Moreton Hampstead	1,543	23	
Ilsington	1,000	10	
Widecombe	744	10	
North Bovey	417	4	
Lustleigh	415	5	
	4,130	52	·83
II. EXPOSED PARISHES (7):			
Ashburton	2,762	75	(13 years, 65 deaths = 15 years, 75 deaths.)
Highweek	2,540	39	
Kingsteignton	1,836	33	
Bishopsteignton	1,085	24	
Broadhempston	525	8	
Bickington	230	6	
Teigngrace	170	6	
	9,148	191	1·38
III. IMPERFECTLY SHELTERED PARISHES (17):			
Bovey Tracey	2,460	44	
Chudleigh	2,003	23	
Kingskerswell	1,030	17	
Ipplepen	824	17	
Dawlish Rural	715	20	
Hennock	685	13	
Haccombe	545	5	
Denbury	516	10	
Stoke	511	10	
Abbotskerswell	431	5	
Manaton	327	5	
Ogwell	310	6	
Ideford	286	1	
Coffinswell	200	3	
Woodland	184	1	
Trusham	161	2	
Buckland	71	1	
	11,259	183	1·08

TABLE IVA.—*Newton Rural District (Dr. Harvey's figures). Phthisis deaths.*

Name of parish.	Estimated population, 1898.	'85.	'86.	'87.	'88.	'89.	'90.	'91.	'92.	'93.	'94.	'95.	'96.	'97.	'98.	'99.	Total.	Rates per 1000 per annum.
Ashburton (only 13 years' record)	2762	11	7	8	3	5	3	2	2	9	5	1	3	6			65 (13 years)	1·8
Abbotskerswell	431	—	1	2	—	—	—	—	—	—	—	—	1	1	—	—	5	·75
Bickington	230	—	—	2	—	—	—	2	—	2	—	—	—	—	—	—	6	1·73
Bishopsteignton	1085	1	2	3	1	3	—	1	—	4	3	3	—	1	—	2	24	1·47
Bovey	2460	3	3	4	5	4	1	5	1	5	3	3	3	3	—	1	44	1·18
Broadhemston	525	1	1	—	—	—	1	1	2	—	1	—	—	1	—	—	8	1·0
Buckland	71	—	—	—	—	—	1	—	—	—	—	—	—	—	—	—	1	·9
Chudleigh	2003	2	1	3	2	2	4	1	—	2	—	2	1	1	—	2	23	·76
Coffinswell	200	—	—	—	—	—	—	—	1	—	1	—	—	—	—	1	3	1·0
Haccombe	545	1	1	1	—	—	—	1	—	—	1	—	—	—	—	—	5	·6
Dawlish	715	3	2	—	1	3	1	1	—	2	1	1	1	3	1	—	20	1·8
Denbury	516	—	1	1	1	—	1	—	1	—	—	—	1	3	1	—	10	1·28
Ogwell	310	—	—	—	1	—	—	—	—	1	1	—	—	—	2	1	6	1·28
Highweek	2540	4	5	4	5	2	4	1	1	—	2	2	3	—	2	4	39	1·0
Hennock	685	2	—	—	—	2	—	2	—	—	3	—	1	1	1	1	13	1·26
Ipplepen	824	1	—	2	2	3	3	2	1	1	2	—	—	—	—	—	17	1·37
Ilsington	1000	1	1	2	1	—	—	—	—	1	1	—	1	—	1	1	10	·66
Ideford	286	—	—	—	—	—	1	—	—	—	—	—	—	—	—	—	1	·23
Kingskerswell	1030	—	—	—	—	1	2	3	1	2	—	3	1	1	2	1	17	1·1
Kingsteignton	1836	3	2	—	4	1	3	6	2	—	4	—	2	1	—	5	33	1·2
Lustleigh	415	1	—	—	1	2	—	—	—	—	—	—	1	—	—	—	5	·8
Manaton	327	—	1	—	—	—	1	1	—	1	—	—	—	1	—	—	5	1·0
Moreton Hampstead	1543	—	—	3	3	2	2	2	1	2	—	—	—	4	2	2	23	·99
Stoke	511	3	—	—	2	—	—	1	1	1	1	—	—	—	—	1	10	1·3
Trusham	161	—	—	—	—	—	1	—	1	—	—	—	—	—	—	—	2	·8
Teignngrace	170	1	—	—	—	3	—	1	—	—	—	—	—	1	—	—	6	2·3
North Bovey	417	—	1	—	—	—	—	—	—	1	—	—	—	1	1	—	4	·6
Widecombe	744	2	1	—	—	—	2	—	—	—	—	1	2	—	1	1	10	·89
Woodland	184	—	—	—	1	—	—	—	—	—	—	—	—	—	—	—	1	·36

TABLE V.—*Okehampton Rural District (influence of shelter from W. and S.W. winds).*

Name of parish.	Population, 1891.	Phthisis deaths in 10 years.	Phthisis death rate per 1000 per annum.
I. SHELTERED PARISHES (7):			
Inwardleigh	519	1	
Monkokehampton	191	0	
Chagford	1,460	12	
Gidleigh	129	0	
Throwleigh	281	3	
Drewsteignton	751	5	
Ashbury	69	0	
	3,400	21	·61
II. EXPOSED PARISHES (11):			
Broadwood Kelly	261	3	
Sampford Courtenay	866	19	
North Tawton	1,737	25	
Spreyton	388	4	
North Lew	714	16	
Highampton	284	7	
Beaworthy	268	4	
Germansweek	211	4	
Bratton Clovelly	487	11	
Bridestowe	586	6	
Sourton	448	9	
	6,250	108	1·72
III. IMPERFECTLY SHELTERED PARISHES (10):			
Meeth	203	1	
Iddesleigh	377	4	
Hatherleigh	1,437	14	
Jacobstowe	222	6	
Exbourne	355	5	
Honeychurch	35	0	
Bondleigh	141	2	
Belstone	181	2	
South Tawton	1,264	19	
Okehampton (rural)	520	8	
	4,735	61	1·28

TABLE Va.—*Okehampton Rural District (Dr. Young's figures). Phthisis deaths.*

Name of parish.	Population, 1891.	1890.	1891.	1892.	1893.	1894.	1895.	1896.	1897.	1898.	1899.	Total.	Rate per 1000 per annum.
North Tawton	1,737	7	3	2	3	2	2	3	1	2	—	25	1·4
Sampford Courtenay	866	3	2	3	3	1	1	4	—	1	1	19	2·1
Bondleigh	141	1	1	—	—	—	—	—	—	—	—	2	1·4
Bratton Clovelly	487	2	3	—	2	1	1	1	—	1	—	11	2·2
North Lew	714	1	2	3	1	2	3	—	1	1	2	16	2·2
Beaworthy	268	1	1	—	1	—	—	—	—	—	1	4	1·4
Highampton	284	2	—	2	—	—	—	—	1	2	—	7	2·4
Jacobstowe	222	1	—	1	1	1	2	—	—	—	—	6	2·7
Hatherleigh	1,437	2	1	—	2	4	1	1	—	2	1	14	·9
Inwardleigh	519	1	—	—	—	—	—	—	—	—	—	1	·2
Iddesleigh	377	2	1	—	—	—	—	—	—	1	—	4	1·0
Chagford	1,460	1	2	2	1	3	1	1	1	—	—	12	·8
Throwleigh	281	1	—	—	—	—	—	1	1	—	—	3	1·0
Sourton	448	2	1	—	4	—	1	—	—	—	1	9	2·0
South Tawton	1,264	1	4	1	1	—	—	4	2	2	4	19	1·5
Bridestowe	586	1	1	2	—	—	—	—	—	—	2	6	1·0
Drewsteignton	751	—	1	—	1	—	1	—	1	—	1	5	·6
Germansweek	211	—	1	—	1	—	—	—	1	—	1	4	1·9
Broadwood Kelly	261	—	1	—	1	1	—	—	—	—	—	3	1·1
Exbourne	355	—	—	1	—	1	—	—	—	1	2	5	1·4
Belstone	181	—	—	—	1	—	—	—	—	1	—	2	1·1
Spreyton	388	—	—	—	—	1	1	1	—	—	1	4	1·0
Meeth	203	—	—	—	—	—	—	—	—	—	1	1	·5
Ashbury	69	—	—	—	—	—	—	—	—	—	—	0	0
Gidleigh	129	—	—	—	—	—	—	—	—	—	—	0	0
Honeychurch	35	—	—	—	—	—	—	—	—	—	—	0	0
Monkokehampton	191	—	—	—	—	—	—	—	—	—	—	0	0
Okehampton (rural)	525	—	1	1	1	4	—	1	—	—	—	8	1·5

TABLE VI.—*Barnstaple Rural District (influence of shelter from W. and S.W. winds).*

Name of parish.	Population, 1891.	Phthisis deaths, 10 years.	Phthisis death rate per 1000 per annum.
I. SHELTERED PARISHES (10).			
Westdown	562	2	
Bittadon	46	0	
Eastdown	346	1	
Kentisbury	344	0	
Arlington	238	0	
Parracombe	318	2	
Brendon	294	0	
Challacombe	226	1	
Highbray	226	2	
Tawstock	1,206	9	
	3,806	17	·44
II. EXPOSED PARISHES (14):			
Morthoe	678	7	
Georgeham	747	9	
Braunton	2,171	26	
Heanton Punchardon	449	4	
Instow	650	8	
Ashford	151	2	
Pilton (rural)	555	7	
Marwood	787	6	
Loxhore	192	3	
Bratton Fleming	499	5	
Stoke Rivers	199	1	
Goodleigh	239	3	
Horwood	108	0	
Newton Tracey	140	2	
	7,565	83	1·1
III. IMPERFECTLY SHELTERED PARISHES (12):			
Westleigh	483	2	
Fremington	1,188	10	
Atherington	475	5	
Bishop's Tawton	781	8	
Swimbridge	1,171	11	
Landkey	647	5	
Berrynarbor	652	2	
Coombe Martin	1,407	11	
Trentishoe	96	1	
Martinhoe	165	1	
Countisbury	233	1	
Sherwell	370	1	
	7,668	58	·75

TABLE VIA.—*Barnstaple Rural District (Dr. Harper's figures). Phthisis deaths.*

Name and parish.	Population 1891.	'90	'91	'92	'93	'94	'95	96	'97	'98	'99	Total.	Rate per 1000 per annum.
Atherington	475	—	1	1	—	—	1	1	—	—	1	5	1·0
Bishop's Tawton	781	2	—	—	2	1	2	—	—	—	1	8	1·0
Fremington	1,188	1	—	1	1	2	—	1	1	2	1	10	·8
Horwood	108	—	—	—	—	—	—	—	—	—	—	0	0
Instow	650	1	—	—	—	2	2	2	—	1	—	8	1·2
Landkey	647	1	—	—	—	2	2	—	—	—	—	5	·7
Newton Tracey	140	1	—	—	—	1	—	—	—	—	—	2	1·4
Swimbridge	1,171	1	1	2	2	1	—	—	2	2	—	11	·9
Tawstock	1,206	1	2	3	1	—	—	1	1	—	—	9	·7
Westleigh	483	—	—	1	—	—	—	—	—	1	—	2	·4
Ashford	151	—	—	—	1	—	—	—	1	—	—	2	1·3
Bittadon	46	—	—	—	—	—	—	—	—	—	—	0	0
Braunton	2,171	2	3	3	3	—	1	4	3	3	4	26	1·1
Georgeham	747	2	1	—	1	—	1	—	—	2	2	9	1·2
Goodleigh	239	—	—	—	—	—	1	—	—	—	2	3	1·2
Heanton Punchardon	449	—	—	—	1	—	1	1	1	—	—	4	·9
Marwood	787	1	1	—	—	—	—	—	1	1	2	6	·7
Morthoe	678	—	1	1	—	—	1	1	—	2	1	7	1·0
Pilton (rural)	555	—	2	—	1	—	—	—	1	3	—	7	1·2
Shirwell	370	—	—	—	—	—	—	—	—	1	—	1	·2
Westdown	562	2	—	—	—	—	—	—	—	—	—	2	·3
Arlington	238	—	—	—	—	—	—	—	—	—	—	0	0
Berrynarbor	652	—	1	—	—	—	—	1	—	—	—	2	·3
Bratton Fleming	499	—	—	—	1	2	—	—	1	—	1	5	1·0
Brendon	294	—	—	—	—	—	—	—	—	—	—	0	0
Challacombe	226	—	—	—	—	—	—	—	—	—	1	1	·4
Countisbury	233	—	—	—	—	—	—	—	—	—	1	1	·4
Combe Martin	1,407	—	1	1	—	3	1	2	—	2	1	11	·7
Eastdown	346	—	—	—	—	—	—	—	—	—	1	1	·2
Highbray	226	2	—	—	—	—	—	—	—	—	—	2	·9
Kentisbury	344	—	—	—	—	—	—	—	—	—	—	0	0
Loxhore	192	—	—	—	—	—	—	2	—	1	—	3	1·5
Martinhoe	165	—	—	—	—	—	—	—	—	—	1	1	·6
Parracombe	318	—	—	1	—	1	—	—	—	—	—	2	·6
Stoke Rivers	199	—	—	—	—	—	1	—	—	—	—	1	·5
Trentishoe	96	1	—	—	—	—	—	—	—	—	—	1	1·0

TABLE VII.—*Soil and phthisis death rate. Soils in the parishes of St. Thomas and Newton Abbot districts.*

Name.	Other soils in parish (lived on).	Number of years recorded.	Phthisis death rate per 1000 per annum.
I. VILLAGES ON CONGLOMERATE:			
Dawlish	A good deal of sandstone, little alluvium, and a little gravel	15	1·8
Stoke in Teignhead	A very little alluvium	15	1·3
Mamhead	Some sandstone	2⅓	Nil.
Ashcombe	A very little alluvium	2⅓	Nil.
Exminster	A little sandstone	2⅓	·5
Powderham	Sandstone, a little river gravel	2⅓	Nil.
Kenn	A very little alluvium and trap	2⅓	Nil.
Haccombe	Some Bovey beds (gravel, sand, clay, lignite).	15	·6
Ideford	Some grits, shales, and alluvium	15	·23
Ide	Some alluvium and shale	2⅓	Nil.
Coffinswell	Many houses on Watcombe clay	15	1·0
Alphington	Many houses on river gravel, some on alluvium	2⅓	·4
Kingskerswell	Some limestone, alluvium, slates, and shales	15	1·1
II. VILLAGES ON SANDSTONE:			
Kenton	Conglomerate, many houses on river gravel	2⅓	1·0
Poltimore	A very few houses on shale	2⅓	Nil.
Pinhoe	Many houses on shale, one on alluvium	2⅓	Nil.
Broadclyst	Light marl, conglomerate, alluvium, river gravel, and pebbles	2⅓	·4
Honiton Clyst	Light marl, alluvium, river gravel, pebbles	2⅓	1·5
Sowton	Light marl	2⅓	Nil.
St. Mary Clyst	Light marl	2⅓	Nil.
Topsham	Conglomerate, many houses on river gravel, a few on alluvium	2⅓	1·5
Clyst St. Lawrence	Alluvium, light marl, conglomerate, shale	2⅓	Nil.
Otterton	Alluvium, gravel, marl	2⅓	2·4
E. Budleigh	No other	2⅓	·5
Bicton	No other (?)	2⅓	3·5
Colaton Raleigh	? —	2⅓	2·8

TABLE VII (*continued*).

Name.	Other soils in parish (lived on).	Number of years recorded.	Phthisis death rate per 1000 per annum.
III. VILLAGES ON LIGHT MARL:			
Clyst Hydon	A few houses on shale and conglomerate	2⅓	1·4
Whimple	Some houses on alluvium	2½	1·4
Rockbeare	Some houses on alluvium, some on river gravel	2½	1·3
Aylesbeare	A very few houses on alluvium, a few on river gravel and pebbles	2⅓	1·0
Farringdon	No other soil	2½	2·0
Woodbury	A good many houses on sandstone, some on pebbles	2½	1·8
St. George's Clyst	Sandstone	2½	Nil.
Lympstone	A very few houses on river gravel	2½	1·1
IV. VILLAGES ON SHALE:			
Tedburn St. Mary	No other soil	2½	1·4
Whitstone	A few houses on alluvium	2½	Nil.
Holcombe Burnell	No other soil	2½	Nil.
Dunsford	A few houses on alluvium	2½	Nil.
Doddiscombsleigh	No other soil	2½	Nil.
Higher Ashton	One house on tufa	2½	2·0
Upton Pyne	Sandstone, river gravel, a little conglomerate	2⅓	·9
Trusham	One house (?) on trap	15	·8
Chudleigh	A few houses on limestone and conglomerate	15	·76
Hennock	A few houses on trap and granite	15	1·26
Bovey Tracey	Granite, alluvium, Bovey beds	15	1·18
Christow	Granite	2⅓	·7
Bishopsteignton	Conglomerate, a few houses on limestone	15	1·47
Ilsington	A very few houses on alluvium	15	·66
Woodland	A very few houses on alluvium	15	·36
Abbotskerswell	Alluvium, conglomerate, limestone	15	·75
Ogwell	Limestone	15	1·28
Highweek	Alluvium, a very few houses on trap and limestone	15	1·0
Bridford	Granite, a few houses on river gravel	2⅓	1·0
Ashburton	Granite	13	1·8
Broadhempston	No other soil	15	1·0
V. VILLAGES ON LIMESTONE:			
Ipplepen	Shale, conglomerate	15	·66
Bickington	Shale	15	1·73
Denbury	Shale, a little alluvium	15	1·28

TABLE VII (*continued*).

Name.	Other soils in parish (lived on).	Number of years recorded.	Phthisis death rate per 1000 per annum.
VI. VILLAGES ON GRANITE:			
Moreton Hampstead	No other soil	15	·99
North Bovey	No other soil	15	·6
Widecombe	No other soil	15	·89
Lustleigh	Some shale	15	·8
Manaton	Some shale	15	1·0
Buckland	Some shale	15	·9
VII. VILLAGE ON TRAP:			
Dunchideock	A few houses on shale and conglomerate	2½	Nil.
VIII. VILLAGES ON RIVER GRAVEL			
Netherexe	No other soil	2½	Nil.
Rewe	Sandstone	2½	Nil.
Stoke Canon	Shale	2½	1·1
Huxham	Shale	2½	4
Brampford Speke	Sandstone, shale	2½	Nil.
IX. VILLAGES ON BOVEY BEDS:			
Teigngrace	No other soil	15	2·3
Kingsteignton	Shale	15	1·2

DISCUSSION

Dr. CAYLEY.—The paper to which we have just listened comprises two interesting points: first, that in certain districts the death rate from phthisis is higher than elsewhere; and secondly, that it is highest in districts exposed to west or south-west winds. I do not, however, think that we are justified in saying that the south-west winds are directly responsible for this difference in the mortality from this cause. I cannot offer any opinion as to the connection between the two things, but some years ago I paid a visit to the Scilly Islands, and I was struck by the considerable number of young people who had died of phthisis, which seemed remarkable in a country with such pure air. In spite of the extreme mildness, however, I noticed that as a general rule doors and windows were closely shut, probably to keep out the winds; consequently, though the people lead an outdoor life, they spend their nights at any rate in unventilated stuffy rooms. Perhaps the influence of the south-west wind may be that people shut it out, and that phthisis obtains not because they get too much of it, but because they do not get enough.

Surgeon-Major A. G. BLACK.—The value of the paper would have been enhanced if the author had given us data concerning the duration of the cases,—whether, for instance, they were more protracted under the influence of the south-west wind and shorter with a west wind. The direction of the wind no doubt brings very different agencies to bear upon the patients. Very properly the author has restricted his paper to the consideration of the death rates. That, of course, does not mean that the phthisis originated in the particular district, for it is obvious that its origin may be altogether different. Tuberculosis prevails in many different countries and climates,—in America and the Cape, for instance, where the winds are different from those of Devonshire, so that evidently wind can only be one of the factors concerned.

Dr. LONGSTAFF.—In phthisis, more so than most diseases, not only the conditions of the external country in which the rural labourer lives must be noted, but also the conditions under which he sleeps, the state of his dwelling, etc. The author has told us nothing about the occupations of the people in these different districts. In some districts there are large numbers of fishermen; that is a very distinct mode of life, and would no doubt have an influence for good or for evil in such a disease as phthisis. Then, too, lace-making is very common, and it was long ago recognised by old investigators that lace-

making is a most potent cause of phthisis. Mining, again, especially metal mining, is well known to increase phthisis mortality. I think that we ought to know something about occupation. That is one reason why value attaches to Dr. Haviland's statistics, for he separated the sexes, and by so doing he largely got over the difficulty referred to, seeing that fishing and mining would exclusively affect men, and lace-making women. Then as to the character of the dwellings: any of us must have noticed that while in some parts the houses are very old and unhealthy, in others they are, comparatively speaking, good. The permeability or impermeability of the soil is certainly a factor of some importance, but this factor may be neutralised by the conditions peculiar to the dwelling itself, so that a house may be damp which theoretically ought to be dry. Anyone who knows Devonshire must be aware of the fact that for dirtiness of the house surroundings the inhabitants are not exceeded by any people except the western Irish. Then there is the question of the distribution of rainfall. This interests me in reference to a paper by the late Mr. Pengelly on the influence of Dartmoor on the climate of Devonshire, in that it drains the air of its rain, leaving a dry district to the east. Then there are differences of race in the Devonshire people, the North Devon people especially being a very marked and characteristic race. I am not an anthropologist myself, and cannot speak *ex cathedrâ* on this point, but it is easy to see that there is a difference between races in respect of their proneness to phthisis, from whatever point of view we regard the heredity of the disease. Beyond the influence of race in the larger sense we get the influence of race in the more restricted sense of families or tribes. They, the Devonshire people, move about the world perhaps more than in other counties, but I doubt whether they move from one village to another so that there is much intermarriage. That may be a subtle cause which it is impossible for us to analyse. Then there is the question of diagnosis. Unfortunately the medical men of Devonshire, like their brethren elsewhere, are not all equally strong in the matter of diagnosis. They have not all even the same notions as to the nomenclature of the disease. It is therefore quite possible that we may get a number of deaths returned in a certain district from phthisis which others would return as pleuritis, etc. Greatly intensifying these sources of fallacy is the fact that the writer of the paper has given us figures extending over a very short series of years, and for small populations. I should have been interested if he had given us in the tables the actual figures, *i. e.* the precise number of deaths in the various districts, because that would have given us some idea of how far they are to be trusted. There are differences, too, in the poor law administration. It may be that in some districts, owing to the influence of a few

individuals, a large number of the moribund may be removed to the county hospital or infirmary, while in the next district the dying would remain at home to die. Lastly, if you arrive at a hypothetical deduction, the best way of confirming it is to look at the facts in order to see if in any way they are explainable. Is there any reason, for instance, why the south-west wind should cause phthisis? We have been given two reasons for this to-day; one that it is due to intercurrent inflammations caused by chills, and the other that people shut themselves up and breathe an impure atmosphere. The latter cause, I suppose, operates throughout the country. The people most exposed by virtue of their occupations are those who shut themselves up at night. I trust that nothing I have said will tend to discourage the author. On the contrary, I hope that these suggestions will encourage him to make further observations.

Sir RICHARD DOUGLAS-POWELL.—It is impossible, without a more accurate knowledge of the country than I possess, to discuss this paper in a way its value would call for. It seems to me that the author has shown with considerable force that the death rate of phthisis is greatly influenced by the prevalence of strong winds. I did not gather that the author means us to understand that there is a mortality from the south-west wind as regards phthisis. I think he means that it is the prevalence of wind which renders phthisis more prevalent. It was only an accident that in the part of England with which he deals west and south-west winds are the prevalent ones. This brings his observations into almost complete harmony with the observations made some years ago by Dr. Haviland, who showed that the windy parts of Great Britain were the parts where phthisis was most prevalent. He showed, moreover, that this prevalence of wind and its relation to phthisis was to be observed in various parts of England and Wales, and therefore that it was not any particular wind, but that the effect was due to great movements of the atmosphere. I quite agree with Dr. Cayley's explanation of the reason why pulmonary tuberculosis is associated with the prevalence of high winds, viz. that it leads the inhabitants to shut up windows and doors, particularly at night. The other causes alluded to by Dr. Longstaff would, I imagine, be causes which would be common to other conditions and situations than those associated with high winds, and, although potent causes of consumption, would not explain why consumption was so common in windy districts. The paper is of great value, but of course it only applies to a small area of country. If we could get similar careful observations made with regard to several important parts of England, I think we should obtain most valuable records for comparison. No doubt the author has carefully studied the very valuable maps of Dr. Haviland, and I fancy they will be found to be very much in

accord with the observations which he has brought forward to-night.

Sir HERMANN WEBER.—Our thanks are due to the author for having undertaken an immense amount of research, an amount of which the length of his paper can convey no adequate idea. The influence of windiness on the mortality from consumption is of the greatest importance, not only from the climatological, but also from the therapeutical point of view. The author says he has undertaken these researches because they have a bearing on the question of sanatoria. The majority of medical men have long observed that windiness most injuriously influences consumptive patients, and in the erection of sanatoria of late that question has been carefully taken into consideration. When walking about Norfolk with Dr. Burton Fanning, looking out for a site, we always looked for a place where a range of downs protected the locality from the sea air. That windiness is a most injurious factor in cases of delicacy of the respiratory mucous membrane is shown from the earliest infancy. I remember a large number of children who, whenever they were exposed to strong winds, became ill, and several of those of them who survived the earlier attacks of bronchitis and pneumonia, succumbed later to consumption. My own experience has been that strong wind from any quarter, not only south and south-west, is injurious to consumptive people, and seems to increase the mortality. If you look at a map of different parts of England or Scotland you will find that the districts where the phthisis mortality is great are intermixed with districts where it is not great. Now these are matters of the greatest interest. When you look into the conditions of these districts with a high phthisis mortality and the districts close by, likewise apparently exposed to the same high wind, you will find that in the latter there is some sort of natural barrier between the wind and the habitations. If you look at the map of the Isle of Man drawn up by Dr. Haviland, you will find that not only the two most southern districts, Rushen and Arbory, are subject to a high mortality, but that those most exposed to north and north-west, viz. Bride and Andreas, are also subject thereto. There is also a district in the middle of the eastern border which is marked deep blue, this being almost the worst colour. The causes which produce a tendency to consumption are so numerous that it is difficult to fix on one in particular. If, however, we consider one by itself, such as exposure to winds, and if we find that certain parts or certain districts are less subject to consumption than others, although on the map they seem to be much exposed, we may find on close examination of the district and neighbourhood that there are circumstances in the local configuration which act as barriers to the wind. On the other hand, if the phthisis mortality is high

in a sheltered and otherwise apparently well-situated locality, we may, by carefully examining, discover that there are other injurious influences, such as swamps, contaminated soil, habitual intermarriage, common in secluded districts, imperfect food, and badly arranged houses.

Dr. Braine Hartnell.—The more one looks into the question of wind exposure in phthisis the more important does it become. At Nordrach Dr. Walther does not care what the rainfall is, but is very emphatic that there should be no wind exposure. At Falkenstein and Hohenhonnef and in all well-chosen sanatoria there are woods, so that patients may have walks in any wind without undue exposure.

Dr. Pye-Smith.—It is obvious that no one contribution of this sort can be complete, and it seems a little hard, when one has devoted immense time and labour to the compilation of facts on a particular subject, to be told to do something else. "When the kings build, the hodmen must carry bricks;" and a great problem of this sort must be attacked by a large number of people, each man bringing his brick towards the great edifice. I would submit that it is misleading to speak of percentages when dealing with small numbers. When dealing with numbers less than a hundred the best plan is to give the numbers themselves. We cannot arrive at any final conclusions from observations on small areas. Phthisis is world-wide, and where there happens to be a place free from the disease, thither invalids flock until it becomes a focus of the disease. Moreover we have two very difficult questions to consider: one is the causes which lead to the occurrence of phthisis, *i. e.* why the bacillus finds a suitable soil; and the other is the mortality of phthisis, *i. e.* the causes which help those who have been infected to get well or otherwise. Probably the causes which conduce to one and the other are very different, and it is difficult to separate the statistics which bear on one or the other subject. As to the evil effect of south-west winds, Dr. Cayley's explanation is, I think, the true one.

Sir William Broadbent.—In a disease of which the causation is so complex there are always openings for uncertainty and fallacy in fixing upon one particular point of causation; and unless we can connect the two facts, the prevalence of this wind and the death rate of phthisis, by something which explains the connection we are still left with a great deal of uncertainty in our minds. Many qualifications have been given by Fellows to-night,—the shutting up of the house as a defence against wind, for instance. That one sees not only as a defence against wind but also against cold, so that severe cold may be one of the elements in the causation of phthisis, because it drives people to shut up their houses and to live in filth and darkness. What we lack is the connecting

link between the prevalence of certain winds and the death rate from phthisis. Dr. Longstaff's remarks are particularly instructive, both from his local knowledge and from his masterly way of illustrating the significance of statistics. There have been so many qualifications suggested that it seems to me we are left very much in the position at which Haviland arrived, that it is windiness in general and not any particular wind which operates so unfavourably on consumptive people, and it probably acts on the death rate of phthisis in both the ways which have been pointed out, by causing shutting up of dwellings and by hastening the rate at which tuberculous disease proves fatal.

Dr. GORDON (in reply).—To have extended the area of my inquiry would have greatly delayed what seemed to me ripe for discussion. I hope in time to examine a larger area, and to discuss in full the points which have been raised. It is impossible to deal with objections finally without devoting to each an elaborate investigation. At the same time it seems to me that, when it has been shown for a period of ten years or over, in three different rural districts in different parts of the county (one inland, two on the coast), mapped out into their constituent parishes, that, with very few exceptions, parishes exposed to west and south-west winds have a relatively high phthisis death rate, whilst parishes sheltered from those winds have a relatively low phthisis death rate, the objections raised lose a great deal of their force. In fact, it seems to me rather difficult to explain away the apparent relation of the death rates to the winds.

I do not at all suggest that in all parts of the world west and south-west winds have the effect which I believe they have in Devonshire. How they produce their effect in Devon I am also not prepared to say; I would rather establish the fact first and explain it afterwards. It is possible that the closure of doors and windows against the winds may have something to do with their result. But I may say—giving it merely as a pious opinion—that I think their injurious influence primarily depends on their prevalence, violence, and wetness. If, however, one were to go on to say that any particular sort of wind promotes phthisis mortality generally, one would impugn the usefulness of many existing health resorts in various parts of the world, and I do not think that at present we have sufficient ground for doing that, though it is significant that Davos and Nordrach, the two most successful phthisis health resorts, have this in common (differing so widely in other ways from each other), that they are peculiarly wind-sheltered.

There are two other points to which I would briefly allude. They are suggestive, but I only give them for what they are worth.

First, in the Royal Devon and Exeter Hospital there are two

wings, a south-west and a north-east. The south-west wing is fully exposed to west and south-west winds; the north-east is well protected from them. When westerly winds have been blowing, my phthisis patients in the south-west wing (men) have generally done badly, but my phthisis patients in the north-east wing (women) have done as well as at other times—very well as a matter of fact.

Secondly, the Valley of Dunchideock on the eastern slopes of Haldon is well protected from west and south-west winds, and one who knows it thoroughly, having long resided there, has told me that "no one catches cold there;" that, although the snow lies longer in winter, the effects of frost on vegetation are far less severe than in the lower lands to the east; and that one case of bad chronic phthisis (in which the diagnosis seems to have been well established) got well there under his own observation,—recovered indeed in the very house which I had already noted as the one best suited for a sanatorium on account of its being absolutely sheltered from west and south-west winds.

Note by Dr. Gordon.

November 21st, 1900.—It may increase any usefulness which my paper possesses if I add a short note with regard to some of the objections raised in its discussion.

My friends, who have already helped me so much with information about their districts, have very kindly furnished me with their experience on these points. In brief, their statements amount to this:

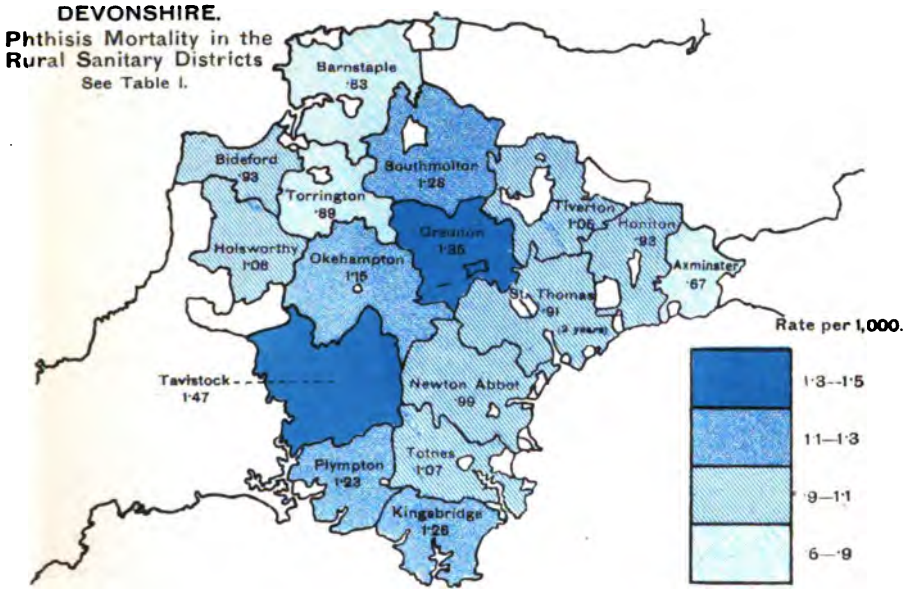
1. In none of the four districts (St. Thomas, Newton Abbot, Okehampton, Barnstaple) do any definite race differences exist. Mr. Baring-Gould has thought a distinct race could be traced in two parishes of Okehampton district, viz. North Lew and Germansweek; yet these parishes merely follow the rule which seems to me to generally obtain.

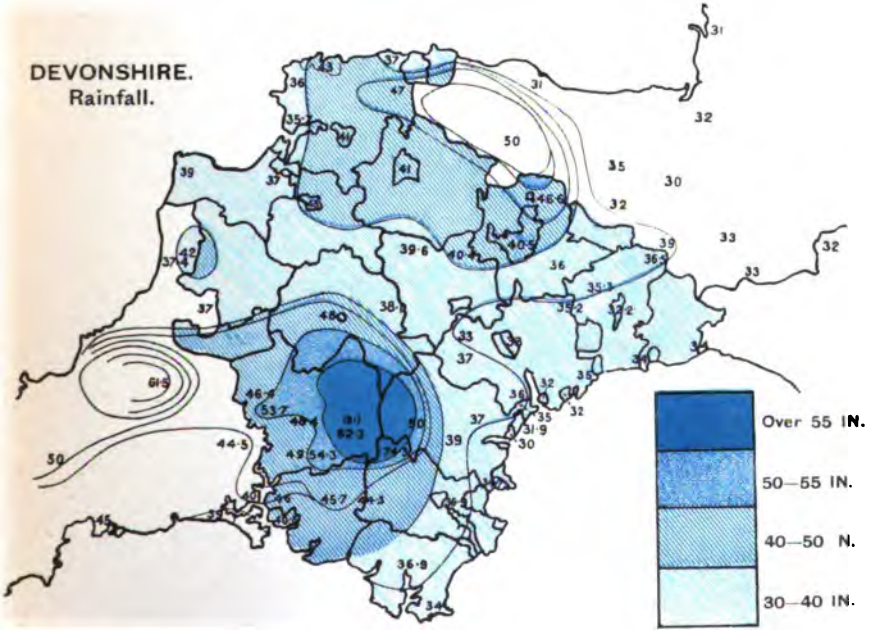
2. In none of the districts can special closeness of intermarriage in certain parishes be considered to exist.

3. In none can the character of the dwellings be considered to vary definitely from parish to parish.

4. In none can differences in phthisis mortality be attributed to differences of occupation, except that it seems that women suffer rather more than men, this being attri-

buted probably to their more indoor life. In North Tawton parish (Okehampton district), there is a woollen manufactory where large numbers of men, women, and children are employed; yet North Tawton has just about the mortality which one would have ventured to predict. Excluding shopkeepers, railway servants, and private residents, the great bulk of the population in these districts is agricultural. Miners do not exist in any of them; nor lacemakers except a few women so employed in the east of St. Thomas district, where no special proclivity to phthisis has been traced amongst them in the period dealt with.





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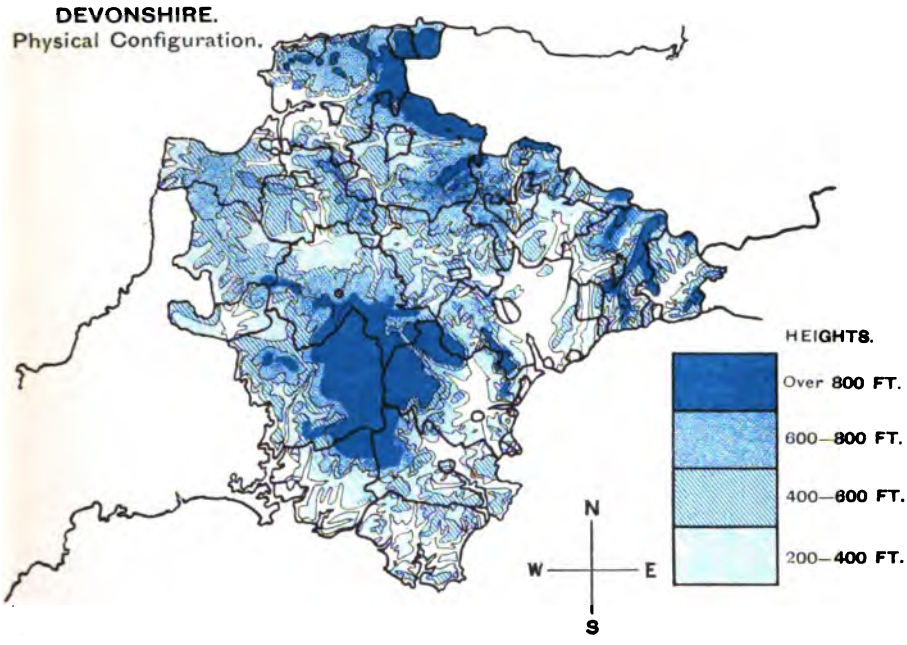

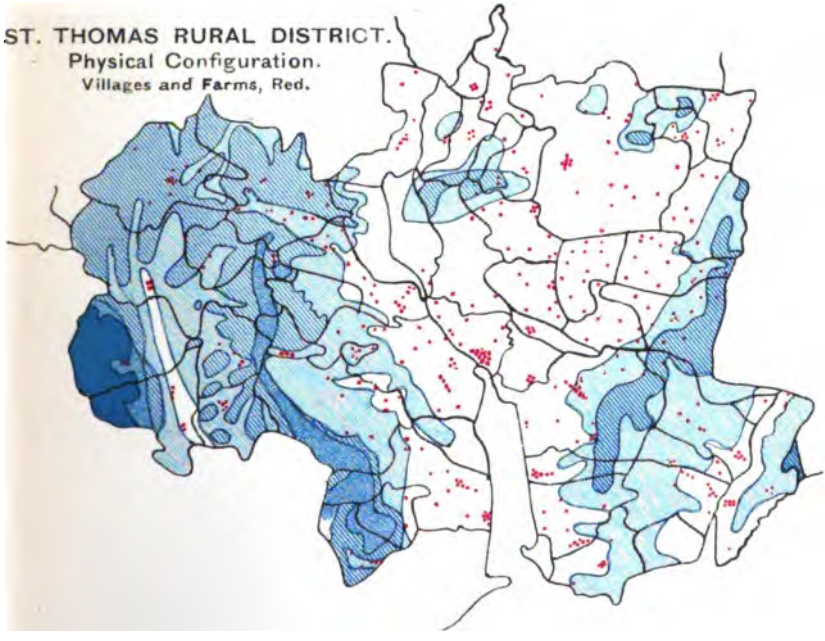

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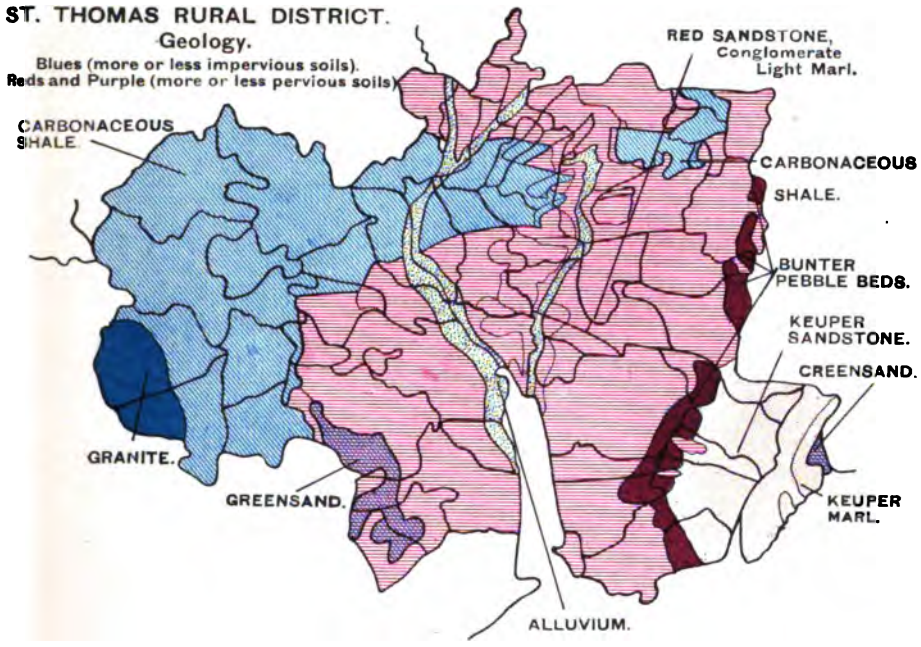

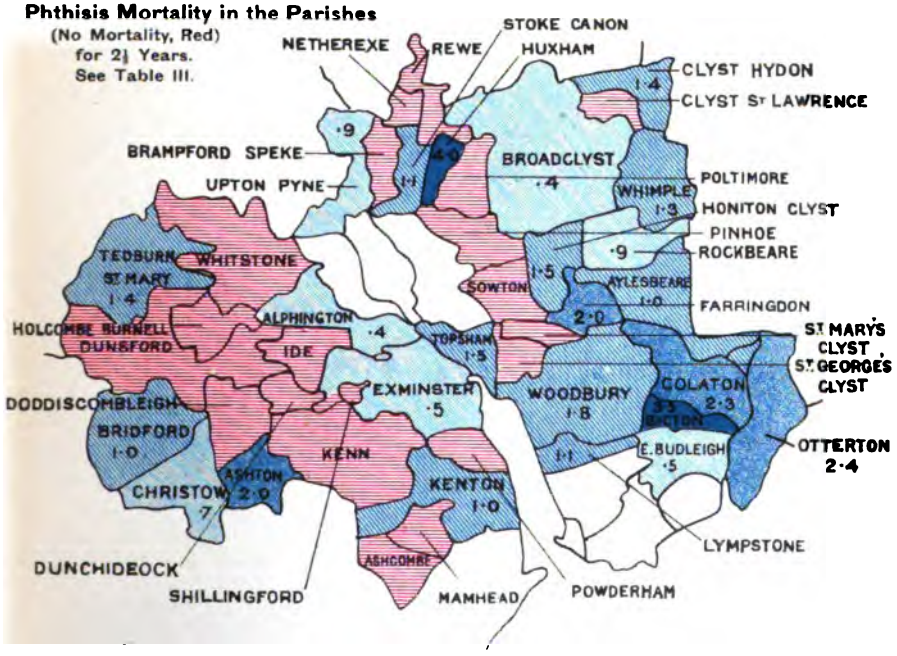

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ON METABOLISM IN PHTHISIS

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THE method of combating tubercular disease, and more especially pulmonary tuberculosis, by over-feeding, has attracted considerable notice of late years; and the opinions of various observers as to its efficacy differ vastly. It occurred to us that it would be interesting, from the scientific as well as from the clinical standpoint, to carry out some research as to the effect of over-feeding on the metabolism of patients suffering from pulmonary tuberculosis. It appeared to us that the best

manner of obtaining definite results would be to take cases of varying severity, and after having determined the metabolism on the diet on which they were ordinarily placed in hospital, to gradually increase the diet in various ways in order to ascertain what was the maximum diet which they could take with advantage, and without causing too great a strain on the organism from a clinical point of view. It seemed to us that one of the most important points to be determined was what number of calories was the most suitable, as this is the easiest method of determining the diet suitable for any given case. The most satisfactory method of obtaining the number of calories per kilo. body-weight suitable for a patient, appeared to be to take his highest known weight, and to calculate the number of calories that he would require in health. From this, it is comparatively easy to make out the sufficient number of calories, so as to ensure that the system of over-feeding—but not necessarily forced feeding—is being carried out. Physiologically it seemed rational to conclude that the system of forced feeding carried out at Nordrach and elsewhere was faulty, as the patients are forced to eat very large quantities of food, quite independently of their subjective symptoms (anorexia, dyspepsia, etc.). We failed to see what benefit the patient could obtain by this system of "cramming," as the strain on the organism must be very excessive; and, as far as the disease was concerned, equally good results could be obtained by studying the individual cases more particularly. There seemed to be no object in compelling a patient suffering from the dyspeptic symptoms so often present in pulmonary tuberculosis to consume, roughly, eighty calories per kilo. body-weight, if the same result could be obtained with a diet containing about sixty calories per kilo. body-weight.

Owing to the kindness of the Committee of the Brompton Hospital we were enabled to carry out this research, to whom—and to Dr. Kingston Fowler for kindly placing a ward at our disposal and for selecting cases for us—we

desire to express our cordial thanks. We are also indebted to Dr. Price, the Assistant Resident Medical Officer, for the trouble he took in superintending the work at the hospital. We also desire to take this opportunity of expressing our cordial thanks to Professor Vaughan Harley for much kind assistance and advice during the progress of this research, which was carried out in his laboratory.

Although for some years there has been a considerable amount of discussion, in both England and Germany, as to whether over-feeding in pulmonary tuberculosis is well founded in a physiological sense, very little work appears to have been undertaken with a view to determining the metabolic condition; and the Russian observers have carried out by far the greater number of researches.

Griezdiev (1) studied the effect of drinking large quantities of hot and cold water in febrile diseases (including phthisis), and states that the nitrogen metabolism was improved qualitatively, and also that the nitrogen was excreted in a more oxidised form.

Kurlov (2), in some experiments regarding the effect of forced feeding by De Bove's method, observes that the metabolism and assimilation of nitrogen was improved, that there was a rapid gain in weight, that the temperature was lowered, and that diarrhœa was relieved. In addition, the general condition improved, as perspiration, cough, and expectoration diminished, and more sleep was obtained. The same observer also states that the forced feeding sometimes changed an excessive excretion of nitrogen into a normal one, or even that a retention of nitrogen followed.

Swavastyanov (3), in studying the effect of food on pulmonary phthisis, found that an increased quantity of nitrogen in the food made very little difference in the amount retained in the body, but that it sometimes converted an excessive waste into a retention of this substance.

Blumenfeld (4) found that the assimilation of fats in this disease was within the normal limits, thus placing on a firm basis the clinical observation that fats are well borne in this disease.

Levin (5), in some observations which he made as to the metabolism in pulmonary phthisis, found that elimination of nitrogen was very low, especially in bad cases, and that the excretion of phosphoric acid was also below the normal quantity, and that this was especially marked in severe cases.

After these preliminary remarks, we now come to consider our own researches into the influence of over-feeding in pulmonary tuberculosis.

Method of Investigation.—During the week previous to the period of the investigation the patients were kept on their ordinary diets, each article of food being separately weighed before it was brought to them, anything that was left over being again weighed. This was done in order to obtain an idea of the quantity of food taken by each patient under normal conditions. Having thus obtained some data, a diet was made out for each patient for the following week, and, on the morning of the fourth day, four drachms of powdered charcoal were given at 8 a.m. The urine was collected in twenty-four hour periods up to 8 a.m. on the eighth day, when four more drachms of charcoal were given. The fæces were collected from the appearance of the first charcoal until the second charcoal appeared.

Then a fresh diet, which had been previously determined upon, was given during the next week, the time and manner of collection remaining the same. A similar plan was followed during the two succeeding weeks, and then the experiment had to be stopped, as some of the patients were leaving the hospital, and we had not sufficient time to spare to make it worth while commencing a second series.

Owing to the difficulty which was experienced in persuading the patient to eat all the diet provided, the

figures given in the tables represent the absolute quantity of the diet constituents taken, the amount ordered being only occasionally eaten. In Periods B, C, and D a weighed quantity of figs and grapes was given, as some of the patients suffered considerably from constipation, and, as will be noticed later, in some of the cases it was necessary to give enemata. (It was decided to take this means of evacuating the large intestine, as it appears to cause as little interference with metabolism as the administration of drugs.)

The total nitrogen was estimated by Kjeldahl's method, no further oxidising agent being employed in the case of the urine, while sodium pyrophosphate was added for the purpose of estimating the oxidation of the fæces.

The quantity of urea was estimated by the sodium hypobromite method.

The method of Gowland Hopkins was used for estimation of the uric acid, ammonia being added to hasten the conversion of this substance into ammonium biurate.

Schlösing's apparatus was employed for the estimation of the quantity of ammonia.

The amount of phosphoric acid was estimated by the uranium nitrate method, and that of the chlorides by precipitating with silver nitrate, and then titrating with potassium sulphocyanide.

The quantity of sulphates in the urine was estimated by Baumann's method—that is, precipitated with barium chloride, and weighing the barium sulphate thus obtained.

The estimation of the quantity of fats in the fæces was made by extraction of the previously acidified dried fæces with ether in Soxhlett's apparatus, the ether extract being dried at 100° C., and weighed after cooling over sulphuric acid.

Two analyses were made in each case, and the average taken, except in the analysis of the sulphates.

In the following description the successive periods are lettered A, B, C, D.

Approximate Diets.—The following can be taken as

the types of diets employed during the different periods, but it should be mentioned that though these were the diets ordered, the patients very rarely took their full quantity of food, so that the quantities actually consumed varied considerably. In consequence of the patients not being able always to eat their full quotient of food, allowance was made for this in calculating the daily diets, and the corrected quantities appear in the metabolism tables.

In Cases 1, 4, 5, and 6, the ordinary diet in use at Brompton Hospital was given in Period A, and this consisted of—

Milk	3 pints.	Bread	8 oz.
Meat	3 oz.	Sugar	1 „
Bacon	1 „	Potatoes and cabbage	4 „
Butter	1 „	Rice pudding	5 „

In addition, during the Period B, the following was given :

Egg	1	Potatoes	2 oz.
Butter	1 oz.	Figs	4 „
Grapes	4 „		

In Period C the diet was altered, so that the patients received :

Milk	4 pints.	Potatoes	2 oz.
Meat	4 oz.	Cabbage	4 „
Bacon	1½ „	Rice pudding	5 „
Eggs	2	Somatose	3 „
Butter	2 oz.	Grapes	4 „
Bread	8 „	Figs	4 „
Sugar	1½ „		

In Period D the diets varied considerably; but the largest given—that of Case 1—was as follows :

Milk	5 pints.	Rice pudding	5 oz.
Chicken	4 oz.	Potatoes	2 „
Bacon	2 „	Cabbage	4 „
Eggs	2	Grapes	4 „
Butter	2½ oz.	Figs	4 „
Bread	11 „	Somatose	3 „
Sugar	3 „	Lactose	1 „

During Periods A and B Cases Nos. 2 and 3 were on the diet that is given in the open-air wards at Brompton Hospital, which consists of—

Milk	3 pints.	Bread	7 oz.
Meat	7 oz.	Sugar	1 „
Egg	1	Potatoes	3 „
Bacon	2 oz.	Cabbage	3 „
Butter	4 „	Rice pudding	3 „

In Period C the diet was altered, so that the following was given:

Milk	4 pints.	Sugar	2 oz.
Meat	7 oz.	Potatoes	4 „
Egg	1	Cabbage	4 „
Bacon	1½ oz.	Rice pudding	5 „
Butter	2 „	Grapes	4 „
Bread	6 „		

The following diet was given during Period D:

Milk	4 pints.	Sugar	3 oz.
Meat	7 oz.	Potatoes	4 „
Egg	1	Cabbage	4 „
Bacon	1 oz.	Grapes	4 „
Butter	1 „	Rice pudding	5 „
Bread	6 „		

Case 1. *Pulmonary Tuberculosis; Acute Infiltration.*

Clinical History.—Age 22, footman. This case was an early one, being only of six months' duration. He was admitted to the special open-air wards on July 18th, 1900, and the following return as to his condition was made at that time:

Left Lung: extensive infiltration in the upper lobe with commencing caseation, and fairly extensive infiltration of the lower lobe.

Right Lung: infiltration of apex of lower lobe and probably early disease of apex of upper lobe.

At the commencement of the research his general condition had improved, the sputum being small in amount, but containing numerous bacilli. The night sweats were very much less marked than when admitted, and the

pyrexia tended to diminish, but oscillated between 99° F. and 100·5° F. The appetite and digestion were good, and the digestive apparatus was in excellent condition, in spite of a tendency to constipation.

He was at least ten kilos. below his highest known weight, but had gained 1·5 kilos. since his admission to the hospital. There was no obvious anæmia, but some dyspnœa. Cough was troublesome, and sleep good. No albumen or sugar was present in the urine.

TABLE 1.—*The various Diets and number of Calories given in Case* 1, *together with the Percentage of Nitrogen and Fats absorbed, etc.*

Period.	A.	B.	C.	D.
Proteids	116·13	137·50	232·50	271·13
Fats	123·28	136·96	183·93	231·22
Carbohydrates . . .	296·71	296·32	321·37	392·17
Total calories . . .	2897·74	3105·96	4126·75	5026·43
Calories per kilo. . .	56·93	59·73	76·28	89·44
Fluids	2029	2204	2810	3444
Nitrogen in urine . .	16·64	14·53	20·82	23·88
Urea „ . .	30·70	28·35	35·56	40·62
Nitrogen in fæces . .	1·62	0·56	2·11	4·36
Fat „ . .	7·94	2·53	3·88	7·85
Nitrogen absorbed, per cent.	91·25	97·45	94·20	89·95
Fat „ „ .	93·82	98·15	97·90	96·41
Weight at end of period .	50·76	52·34	54·36	55·16

Period A.—During this week the patient was kept on the same diet on which he had been since admission, and on which he had decidedly improved. This consisted of a normal quantity of proteids (116·13 grammes), a slightly increased amount of fats (123·28 grammes), and a somewhat small amount of carbohydrates (296·71 grammes). The total number of calories contained in this diet was 2897·74, and was high, considering the fact that the patient was kept in bed. The number of calories per kilo. body-weight was 56·93.

Owing to the fact that a considerable quantity of nourishment was taken in the form of milk, the daily

quantity of fluid was high, being 2029 c.c., and the fluctuations seen in the tables were due to the fact that it was necessary to give more water on some days than on others.

On this diet a daily average of 18·58 grammes of nitrogen was ingested, and since the total quantity of this substance found in the urine was 16·64 grammes, and in the fæces 1·62 grammes, it will be seen that only 0·32 gramme were retained in the body, so that the patient was practically on nitrogen equilibrium.

The average daily excretion of urine was 1653 c.c., and this can be considered the normal amount in health.

The average specific gravity was 1016.

TABLE 2.—*The Daily Excretion of Nitrogen and Nitrogenous Substances in the Urine in Case* 1 *on Diet A.*

Date.	Nitrogen.	Urea.	Uric acid.	Ammonia.
8— 9	16·26	34·02	0·81	0·30
9—10	13·09	21·19	0·55	0·16
10—11	19·34	34·97	1·00	0·43
11—12	17·85	32·62	1·00	0·29
Average	16·64	30·70	0·84	0·30

The average daily elimination of nitrogen in the urine was 16·64 grammes, and was distributed amongst the nitrogenous substances, so that 86·12 per cent. was excreted in the form of urea, 1·68 per cent. in the form of uric acid, and 1·48 in the form of ammonia. From this it will be seen that 11·21 per cent. was excreted as nitrogen rest [1] a quantity which is well within the normal limits.

The absolute excretion of the nitrogen-containing substances in the urine was, taking the average of the twenty-four days, 30·70 grammes urea, 0·84 gramme

[1] It has been shown by v. Noorden ('Path. d. Stoffwechsels,' p. 62) that 84 to 87 per cent. of the nitrogen is in the form of urea, 2 to 5 per cent. in the form of ammonia, 1 to 3 per cent. in the form of uric acid, and 7 to 10 per cent. in the form of nitrogen rest, or in the form of extractions, such as xanthines, hypo-xanthine, creatin, hippuric acid, and colouring matters.

uric acid, and 0·30 gramme ammonia. All these quantities are within the normal amounts except that of uric acid, which is rather high, considering the quantity of fluid taken.

TABLE 3.—*The Daily Excretion of the Inorganic Substances in the Urine in Case* 1 *on Diet A.*

Date.	Phosphoric acid.	Chlorides.	Sulphates.			
			Total.	Alkaline.	Aromatic.	Ratio.
8— 9	2·63	4·62	3·20	2·92	0·28	11·1 : 1
9—10	1·58	4·63	2·66	2·50	0·16	14·4 : 1
10—11	3·33	7·84	3·58	3·30	0·20	16·9 : 1
11—12	2·27	6·02	3·21	3·00	0·21	14·3 : 1
Average	2·45	5·78	3·16	2·95	0·21	14·0 : 1

On turning now to consider the inorganic constituents of the urine, it will be seen that the excretion of phosphoric acid was about the normal—except on the second day, when the quantity eliminated was small,—and that the daily average was 2·45 grammes. The average elimination per diem of chlorides was 5·78 grammes, this being apparently due to the considerable increase found on the third and fourth days, and is about that found in normal individuals.

The quantity of sulphates excreted in the urine showed a daily average of 3·16 grammes, and was about the normal quantity, thus showing that there was an active proteid metabolism going on in the body. The quantity of alkaline sulphates contained in this amount was 2·95 grammes, so that 0·21 gramme were excreted in the form of aromatic sulphates, this latter figure being about the quantity which has been found by one of us (G—), in conjunction with Professor Vaughan Harley (6), to be the amount normally excreted. The ratio of the alkaline to the aromatic sulphates was 14 : 1, showing that there was no increased intestinal putrefaction occurring during this period.

TABLE 4.—*The Daily Excretion of Nitrogen and Fats in the Fæces in Case* 1 *on Diet A.*

Date.	Quantity.	Water per cent.	Nitrogen.	Fats.
8— 9	520	80·91	3·27	16·11
9—10	102	93·09	0·23	1·14
10—11	410	89·01	1·49	7·26
11—12	410	89·01	1·49	7·26
Average	361	87·26	1·62	7·94

The average daily elimination of nitrogen in the fæces was high, being 1·62 grammes, and this was due to the fact that it was necessary to administer enemata on two occasions, owing to the constipation becoming much more marked. On referring to the complete metabolism Tables (see Appendix), it will be seen that the quantity of this substance eliminated in the fæces belonging to the first day was very large, and, although the amount passed on the second day was very low, this was followed by a high excretion on the third and fourth days. As the second enema given brought away the fæces belonging to these two days, it has been considered advisable to divide the quantity by two, so as to obtain the approximate absorption for these days. The remarks about the action of the enemata increasing the quantity of nitrogen in the fæces apply also to the fats, and the average daily elimination of this substance was high, being 7·94 grammes. The quantity passed on the first day (16·11 grammes) was extremely large, and accounts, in a great measure, for this high average.

TABLE 5.—*The Daily Diet and Percentage of Nitrogen and Fats absorbed in Case* 1 *on Diet A.*

Date.	Nitrogen in diet.	Fats in diet.	Nitrogen absorbed per cent.	Fats absorbed per cent.
8— 9	18·59	123·55	82·41	86·99
9—10	18·90	123·66	98·78	99·08
10—11	18·43	123·48	91·91	94·12
11—12	18·40	122·44	91·91	94·07
Average	18·58	123·28	91·25	93·82

The average quantity of nitrogen absorbed per diem was considerably below the normal, being only 91·25 per cent., this being accounted for by the large quantity eliminated in the fæces.[1] The average quantity of fats absorbed per diem was 93·82 per cent., a quantity considerably below the normal amount—in direct opposition to what was found,—as will be noticed later, in the other periods.

His weight remained almost stationary during this period, and on the last day was 50·76 kilos., the average for the four days on which analyses were made being 50·90 kilos.

Clinically, the patient did very well on this diet, and took his food very well. There was no apparent bad symptom, except that he suffered considerably, as already mentioned, from constipation, for the relief of which it was necessary to employ enemata.

Period B.—During this week it was decided to keep the patient on practically the same diet as the above, but as beef (which was substituted for the mutton given in period A) contains a greater quantity of proteid and fat, the amount of these two latter substances taken shows a slight increase. In addition to the grapes and figs already mentioned, 280 c.c. of hot water was ordered to be taken every morning, to combat the constipation. These measures resulted in a slight increase of appetite, and consequently the various constituents of the diet were as follows:—proteids, 137·50 grammes; fats, 136·96 grammes; and carbohydrates, 296·32 grammes. The total number of calories contained in this diet was 3105·96, as compared with 2897·74 in period A; and the average number of calories per kilo. body-weight increased to 59·73, notwithstanding the fact that there was a considerable increase in weight during this period.

Although 280 c.c. of water was ordered in addition to the quantity of milk to be taken each day, the increase in

[1] The views as to there being an absorption and re-excretion of nitrogen in the intestines have not been taken into account in this connection.

the quantity of fluids was only trifling, as the patient did not take so much water at other times; and the average quantity drunk daily was 2204 c.c., as compared with 2029 c.c. in the previous period.

The average daily quantity of nitrogen taken in the diet during this week was 22·00 grammes; and since 14·53 grammes of this substance was passed in the urine, and 0·56 gramme in the fæces, it will be seen that 5·91 grammes were retained in the body—a very different condition to that of period A, when the patient was on nitrogen equilibrium.

Notwithstanding the increased quantity of fluids taken, the average daily excretion of urine diminished to 1493 c.c., as compared with 1653 c.c. in the previous week—a decrease which cannot be accounted for by the fact that there was an increase in the night sweats, or any sensible perspiration at any other time. The average specific gravity declined during this period from 1016 to 1015.

TABLE 6.—*The Daily Excretion of Nitrogen and Fats in the Fæces in Case* 1 *on Diet B.*

Date.	Nitrogen.	Urea.	Uric acid.	Ammonia.
15—16	15·23	27·66	0·66	0·23
16—17	17·75	35·82	0·71	0·34
17—18	12·45	—	0·65	0·19
18—19	12·69	23·05	0·55	0·30
Average	14·53	28·84	0·64	0·27

As was indicated by the lowered specific gravity, the average daily excretion of total nitrogen in the urine diminished, despite the increased quantity given in the food, and was 14·53 grammes as compared with 16·64 grammes in period A. This quantity of nitrogen was distributed amongst the nitrogen-containing substances in the urine as follows:—87·92 per cent. was excreted in the form of urea,[1] 1·49 per cent. in that of uric acid, and 1·51 per

[1] Owing to neglect in repeating the estimation on the third day of the analytical period, the result obtained on this day being too high had to be

cent. in that of ammonia; the proportion excreted as nitrogen rest being 9·08 per cent. This latter percentage is still within the normal limits, and compares with 11·21 per cent. in the previous period.

As has already been mentioned, only three days' analyses of the quantity of urea are available; but the average excretion per diem was 28·84 grammes, as compared with 30·70 grammes during the previous week. The average daily excretion of uric acid also showed a diminution, from 0·84 gramme to 0·64 gramme; and that of ammonia a slight decrease, from 0·30 gramme to 0·27 gramme.

TABLE 7.—*The Daily Excretion of the Inorganic Substances in the Urine in Case* 1 *on Diet B.*

Date.	Phosphoric acid.	Chlorides.	Sulphates. Total.	Alkaline.	Aromatic.	Ratio.
15—16 .	2·45	4·90	2·69	2·53	0·16	15·8 : 1
16—17 .	2·26	3·05	1·99	1·75	0·24	7·3 : 1
17—18 .	2·12	6·13	2·82	2·62	0·20	13·1 : 1
18—19 .	1·90	5·94	2·89	2·69	0·20	13·5 : 1
Average	2·18	5·01	2·60	2·40	0·20	12·0 : 1

Having discussed the excretion of the nitrogenous constituents of the urine, we now turn to the inorganic substances, and it will be noticed that the average daily elimination of phosphoric acid diminished from 2·45 to 2·18 grammes. The chlorides also shared in the generally lessened excretion noticed in the other substances analysed for; and the daily average elimination was 5·01 grammes, as compared with 5·75 grammes in the previous period.

The average excretion of the total sulphates in the urine per diem showed a decided diminution, being only 2·60 grammes, as compared with 3·16 grammes in period A; and the decline in the quantity of the alkaline sulphates was proportionately greater than that of the aromatic sul-

omitted, and consequently the figures given above are the average of only three days.

phates, the former diminishing from 2·95 grammes to 2·40 grammes, while the latter only decreased from 0·21 grammes to 0·20 grammes. Consequently, the ratio between these two substances was 12 : 1, as compared with 14 : 1 in the previous week.

Decrease of phosphates, chlorides, and sulphates, together with the nitrogen, is no doubt due to the building up of tissue proteids in the patient.

TABLE 8.—*The Daily Excretion of Nitrogen and Nitrogenous Substances in the Urine in Case* 1 *on Diet B.*

Date.	Quantity.	Water per cent.	Nitrogen.	Fats.
15—16	103	78·87	0·72	3·27
16—17	103	78·87	0·72	3·27
17—18	72	92·88	0·17	0·75
18—19	48	59·96	0·63	2·83
Average	82	77·65	0·56	2·53

On turning to the consideration of the fæces, it will be noticed, on referring to the table given above, that there was a marked diminution in the quantity of nitrogen excreted, the daily average amount during this week being only 0·56 gramme, as compared with 1·62 grammes in period A. The explanation of this great difference is to be found in the fact that there was no necessity to administer enemata during this week, and, consequently, there was no excessive excitation of the intestinal walls. For the same reason the average excretion of fats per diem decreased from 7·94 grammes to 2·53 grammes.

TABLE 9.—*The Daily Diet and Percentage of Nitrogen and Fats absorbed in Case* 1 *on Diet B.*

Date.	Nitrogen in diet.	Fats in diet.	Nitrogen absorbed per cent.	Fats absorbed per cent.
15—16	21·84	136·89	96·70	97·61
16—17	21·69	136·82	96·68	97·61
17—18	22·31	137·10	99·24	99·45
18—19	22·16	137·03	97·16	97·93
Average	22·00	136·96	97·45	98·15

Corresponding to the diminution in the quantity of nitrogen found in the fæces (noted above), and due also to the fact that the quantity of proteids given in the diet was increased, there was a marked rise in the average amount of nitrogen absorbed—97·45 per cent., as compared with 91·25 per cent. in the previous period. This was a very good rate of absorption, especially when it is remembered that the patient was taking a considerable quantity of fat. The average rate of absorption of fat also increased decidedly, and reached the normal limits, being 98·15 per cent., as against 93·82 per cent. in period A.

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The condition of the patient clinically was very favourable, as he took his food better, and constipation was absent, there being also a decided gain in weight.

Period C.—Since in the first period it had been necessary to administer enemata, it had been considered advisable, as already mentioned, to obtain practically another normal period in this case; and, in this period, it was decided to test the effect of a marked increase in the quantity of food given. The diet was so arranged that the given increase was made in the proteids and in the fats, as we were anxious to keep the quantity of carbohydrates as near the previous amount as was practicable. The most convenient way to obtain this end was to increase the quantity of milk, as we did not wish to use a very excessive quantity of concentrated foods. The concentrated food employed in these experiments was somatose, and, both on the grounds of expense and for the future practical value of our results, it was not advisable to make too great use of it.

The quantity of proteids was accordingly increased by almost 60 per cent, to 232·50 grammes, and 72 grammes of somatose were given per diem in order to effect part of this large increase. The fats were also increased in nearly the same proportion, as 183·93 grammes were given on an average, while the quantity of carbohydrates increased from 296·32 grammes to 321·37 grammes. The total number of calories was thus increased by, roughly, 25 per cent., as 4126·75 were contained in this diet, as compared with

3105·96 in period B. Despite a further marked rise in weight, the average number of calories per kilo. body-weight was increased to 76·28—a very large number when it is remembered that the patient was at rest in bed.

The daily quantity of fluids taken was increased to 2810 c.c., partly owing to the increased amount of milk given, and partly due to the fact that the patient desired a larger quantity of water.

The amount of nitrogen contained in the proteids given during this period averaged 37·20 grammes; and the average amount of this substance recovered from the urine was 20·82 grammes, and from the fæces 2·11 grammes. Therefore 14·27 grammes were retained in the body. Though this is absolutely a large increase over the quantity (5·91 grammes) retained on an average during period B, it will be seen later that the increase is proportionately small, and at a great expenditure of food, when the greatly increased quantity of nitrogen given in the diet is taken into consideration.

The daily average excretion of urine was 1957 c.c., and although this is a marked increase over the quantity found in the last period, still the increase is not so marked as would be expected from the extra quantity of fluid taken. The increase in the quantity of urine not keeping pace with that of the fluids was noticed in all the cases, even when (as in this case) there was no increase, or even diminution, in the amount of night sweat. The average specific gravity remained practically the same, being 1014.

TABLE 10.—*The Daily Excretion of Nitrogen and Nitrogenous Substances in the Urine in Case* 1 *on Diet C.*

Date.	Nitrogen.	Urea.	Uric acid.	Ammonia.
22—23 .	18·98 ...	30·59 ...	0·60 ...	0·16
23—24 .	23·58 ...	42·11 ...	0·84 ...	0·23
24—25 .	18·26 ...	33·69 ...	0·51 ...	0·14
25—26 .	22·34 ...	35·85 ...	0·88 ...	0·30
Average .	20·82 ...	35·56 ...	0·71 ...	0·21

The amount of total nitrogen excreted in the urine averaged 20·82 grammes per diem, and showed a marked increase over that of period B, when it was only 14·53 grammes. The total nitrogen was distributed so that 79·88 per cent. was excreted as urea (a marked decrease from the 87·92 per cent. excreted in this form in period B), while 1·12 per cent. was excreted as uric acid, and 0·81 per cent. as ammonia, the percentage of these two latter substances also showing a decrease. The amount excreted as nitrogen rest increased very markedly, being 18·19 per cent., and appears to suggest a greatly diminished power of elaboration by the liver.

The average daily excretion of urea rose from 28·84 grammes in period B, to 35·56 grammes in this period; and that of uric acid from 0·64 grammes to 0·71; while that of ammonia decreased from 0·27 grammes to 0·21 grammes.

TABLE 11.—*The Daily Excretion of the Inorganic Substances in the Urine in Case* 1 *on Diet C.*

Date.	Sulphuric acid.	Chlorides.	Sulphates.			
			Total.	Alkaline.	Aromatic.	Ratio.
22—23 .	2·34	6·80	4·75	4·52	0·23	19·9 : 1
23—24 .	3·11	13·44	3·96	3·45	0·51	6·8 : 1
24—25 .	2·95	8·11	2·90	2·68	0·22	12·2 : 1
25—26 .	3·26	7·41	2·89	2·64	0·25	10·5 : 1
Average .	2·92	8·94	3·62	3·32	0·30	12·4 : 1

On turning to the consideration of the inorganic substances in the urine, it will be noticed that the average excretion of phosphoric acid per diem showed a marked increase over that of the previous period, as, in this case, the average was 2·92 grammes, as compared with 2·18 grammes. The average daily excretion of the chlorides was 8·94 grammes, showing a very marked increase over that in the previous period, when it was 5·01 grammes. This marked rise in the quantity of the chlorides on increasing the quantity of the food is to be noticed in several of the cases; but, as will be seen later, it is not always main-

tained, and is difficult to explain, especially when, as in this case, the most marked increase occurs on the second day of analysis—that is, on the fifth day of the increased diet.

There was a very marked rise in the average daily excretion of total sulphates (3·62 grammes), pointing to an increase in proteid metabolism; and, of this quantity, the alkaline sulphates are represented by 3·32 grammes; therefore, the average amount of the aromatic sulphates excreted was 0·30 grammes—a quantity rather above the normal, and indicating the onset of the increased intestinal putrefaction, which became so marked in the next period. Despite the increase in the quantity of these substances, the ratio of the alkaline to the aromatic remained practically the same as in period B, being 12·4 : 1.

TABLE 12.—*The Daily Excretion of Nitrogen and Fats in the Fæces in Case* 1 *on Diet C.*

Date.	Quantity.	Water per cent.	Nitrogen.	Fats.
22—23	186	67·57	3·43	5·07
23—24	164	81·23	1·75	2·59
24—25	137	69·26	2·34	4·94
25—26	58	60·05	1·32	2·93
Average	136	69·50	2·11	3·88

Although in this period there was no disturbing factor, such as the administration of enemata, the average quantity of nitrogen excreted per diem in the fæces was very markedly increased, being 2·11 grammes, as compared with 0·56 grammes in period B. As this figure is, roughly, double the normal amount passed in the fæces, it appears to indicate that the intestinal tract was not able to deal properly with so large a quantity of proteid food. On the other hand, the results obtained in the analysis of the fats in the fæces show that the average daily excretion was 3·88 grammes—that is to say, well within the normal limits. Therefore, the intestinal tract still retained its power of dealing with the fat constituents of the food, al-

though the proteid constituents were not being properly utilised.

TABLE 13.—*The Daily Diet and percentage of Nitrogen and Fats absorbed in Case* 1 *on Diet C.*

Date.	Nitrogen in diet.	Fats in diet.	Nitrogen absorbed per cent.	Fats absorbed per cent.
22—23	37·21	186·80	90·78	97·29
23—24	37·21	186·80	95·83	98·61
24—25	37·37	186·87	93·74	97·36
25—26	37·07	175·23	96·44	98·33
Average	37·21	183·93	94·20	97·90

Despite the great increase in the amount of proteids given in the diet, the quantity of nitrogen absorbed only averaged 94·20 per cent. per diem, this also showing that the intestinal tract was being over-taxed by the excessive quantity given. The average absorption of the fats was 97·90 per cent.—nearly the same as in the previous week. This latter percentage confirms the well-known clinical fact, that patients suffering from pulmonary phthisis are able to deal satisfactorily with a diet containing large quantities of fats.

On the last day of this period, the patient's weight was 54·36 kilos.—an increase of 2·02 kilos. over that of the corresponding day of period B, and an increase of 3·60 kilos. over that of period A; while the average weight of the four days on which he was on analysis was 54·1 kilos., as compared with 52·0 kilos. and 50·9 kilos. respectively of the former periods.

The clinical report of this period was that the patient had difficulty in finishing the required quantity of food, and that he complained of unpleasant subjective symptoms after meals, such as fulness, heaviness, etc.

Period D.—During this week it was decided to make a general increase in the various constituents of the diet, and, so as to avoid too excessive a bulk, it was necessary to fall back on some concentrated foods. For this reason the

72 grammes of somatose given each day during period C were continued, and also the quantity of sugar was increased. In addition 28 grammes of lactose were given, to assist in attaining the increased quantity of carbohydrates. A larger quantity of milk was also given. The average amount of proteids consumed under these circumstances was 271·13 grammes, an increase over that of period C of 38·63 grammes; while the fats increased from 183·93 grammes to 231·22 grammes—that is to say, to 2½ times the usual quantity. The average quantity of carbohydrates taken per diem rose from 321·37 grammes to 392·17 grammes, some of this increase being effected, as above mentioned, by means of sugar and lactose, in order to avoid intestinal irritation from the excessive bulk. The total number of calories contained in this enormous diet was naturally very large, amounting to 5026·43, as against 4126·75 in period C, and was, approximately, 2000 more than in the first two periods. Although there was a further decided increase in weight, the average number of calories per kilo. body-weight rose to the very high value of 89·44. Owing to a further increase in the quantity of milk taken per diem, the average quantity of fluids was 3444 c.c.

The amount of nitrogen contained in the average quantity of proteids given was 43·38 grammes, and since the total amount of nitrogen found in the urine was 23·88 grammes, and in the fæces 4·35 grammes, it follows that 15·65 grammes were retained in the body—a very slight increase over period C, when it is remembered that more than 6 grammes extra of nitrogen were given in the food, representing no less than 37·50 grammes of proteids.

The average quantity of urine passed per diem rose further, to 2288 c.c., but still was decidedly beneath the quantity of fluids taken, and the disparity tended to become more and more marked the greater the increase in the quantity of fluids. This difference between the quantity of fluid taken and the quantity excreted as urine may be explained by the kidneys ceasing to become stimulated by the increased quantity of the nitrogenous constituents of

the urine, and this appears to be borne out by the fact that the specific gravity diminished to 1012.

TABLE 14.—*The Daily Excretion of Nitrogen and Nitrogenous Substances in the Urine in Case* 1 *on Diet D.*

Date.	Nitrogen.	Urea.	Uric acid.	Ammonia.
29—30	23·33	36·95	0·87	0·30
30—31	24·24	43·35	0·83	0·31
31—1	22·46	38·44	0·73	0·20
1—2	25·38	43·72	0·84	0·68
Average	23·88	40·62	0·82	0·39

The average excretion of total nitrogen in the urine rose to 23·88 grammes, a proportionately greater increase than that of the previous period, when the respective increase in the quantity given in the food is taken into consideration. The average proportion of total nitrogen excreted as urea was 79·33 per cent., practically the same as in period C, both being considerably below the normal. The proportion excreted in the form of uric acid remained almost the same (1·44 per cent.), while that in the form of ammonia was almost double the previous quantity, being 1·45 per cent., as compared with 0·81 per cent. in period C. The quantity excreted as nitrogen rest remained about the same (18·08 per cent.), and points to the lessened power of elaboration and oxydation noticed in the last period. As indicated in the account of the percentage of nitrogen in the forms of urea and uric acid, both these substances showed a proportionate increase to that of the total nitrogen in the urine, the average daily quantity of the former being 40·64 grammes, and of the latter 0·82 grammes. The average daily excretion of ammonia, however, showed a marked increase, being 0·39 grammes as compared with 0·21 grammes in the previous period, thus indicating a diminished alkalinity of the blood.

TABLE 15.—*The Daily Excretion of Inorganic Substances in the Urine in Case* 1 *on Diet D.*

Date.	Phosphoric acid.	Chlorides.	Sulphates.			
			Total.	Alkaline.	Aromatic.	Ratio.
29—30 .	2·08 ...	9·27 ...	3·90 ...	3·39 ...	0·51 ...	6·6 : 1
30—31 .	2·03 ...	7·87 ...	4·52 ...	4·02 ...	0·50 ...	8 : 1
31—1 .	3·67 ...	4·75 ...	4·08 ...	3·63 ...	0·45 ...	8·1 : 1
1—2 .	3·64 ...	11·71 ...	4·59 ...	4·09 ...	0·50 ...	8·1 : 1
Average .	2·86 ...	8·15 ...	4·27 ...	3·78 ...	0·49 ...	7·7 : 1

Having above shortly discussed the behaviour of the nitrogenous constituents of the urine during this very large diet, it is now necessary to turn to the inorganic constituents of the urine, and we find that the average daily excretion of phosphoric acid was very much the same as in period C, being 2·86 grammes, the further increase in the diet not having the effect noticed in comparing periods B and C. The same result is to be seen in the average excretion of the chlorides in this substance. However, the decrease was more marked since, in this period, the average daily excretion was 8·15 grammes, as compared with 8·94 grammes in the previous week; there being, therefore, an absolute diminution in the quantity found. The average excretion of total sulphates in the urine per diem showed a further rise to 4·27 grammes, indicating a continued activity in proteid metabolism. But, as 0·49 grammes of this amount represented aromatic sulphates, as compared with 3·78 grammes of the alkaline sulphates, it will be seen that the tendency to increased putrefaction noticed in the last period had greatly increased, and that the intestinal tract was thus confessing its inability to deal properly with the enormous quantity of food provided. This is easily seen on comparing the ratio of the alkaline to the aromatic sulphates (7·7 : 1) with that of the previous period (12·4 : 1).

TABLE 16.—*The Daily Excretion of Nitrogen and Fat in the Fæces in Case* 1 *on Diet D.*

Date.	Quantity.	Water per cent.	Nitrogen.	Fats.
29—30	200	64·25	3·79	6·67
30—31	235	66·97	4·11	7·24
31—1	303	67·35	5·24	9·89
1—2	252	67·70	4·31	7·59
Average	248	66·02	4·36	7·85

On turning to the consideration of the fæces, the first point to be noted is the enormous increase in the quantity of nitrogen excreted in this manner, the daily average rising to no less than 4·36 grammes as compared with 2·11 grammes in period C. This great increase was entirely due to the diminished absorptive power of the intestines, as no purgatives or enemata were given to hasten peristalsis; and in all probability explains the increased putrefaction in the intestines, indicated in a striking manner by the analysis of the aromatic sulphates. If the increase in the quantities of fats given in the food be taken into consideration, the larger average daily excretion (7·85 grammes) is not surprising, and indicates that the intestinal tract is capable of dealing satisfactorily with large quantities of this substance, even though the amount of putrefaction going on there be very considerable.

TABLE 17.—*The Daily Diet and percentage of Nitrogen and Fat absorbed in Case* 1 *on Diet D.*

Date.	Nitrogen in diet.	Fats in diet.	Nitrogen absorbed per cent.	Fats absorbed per cent.
29—30	43·65	232·86	91·32	97·14
30—31	43·21	238·49	90·49	96·96
31—1	43·65	232·86	87·99	95·75
1—2	43·02	221·08	89·98	96·57
Average	43·38	231·32	89·95	96·41

The quantity of nitrogen contained in the fæces indicated that the absorption of this substance was diminished;

but the daily average found (89·95 per cent.) was much below that to be expected, considering the very large quantities of proteids given in the diet, and shows to what a large extent this substance was wasted. The average absorption of fats showed a further slight diminution, being 96·41 per cent., as compared with 97·90 per cent. in period C; but this amount is only slightly below the normal limits.

On the last day of this period the patient's weight was 55·16 kilos.—that is, an increase of 1·80 kilos. over the corresponding day of the previous period. The average weight of the four days on which analysis was carried out was 56·1 kilos., a gain of 2·0 kilos. over that of period A.

The clinical report of this week was that the patient was by no means so well, that pain and feelings of distension after food had markedly increased, and that other dyspeptic symptoms were more marked; his appetite had failed completely, and he said that he felt utterly unable to continue on the same diet.

Summary.—This patient was confined to bed throughout the time that we are concerned with, and while he was under observation, was considerably below his normal weight, though he was steadily improving in his general condition. During period B the diet was maintained at a slightly higher level than in period A, but was still practically a normal diet for a phthisical patient undergoing open-air treatment, and has been taken as a basis for comparison, as period A was not suitable for this purpose on account of the administration of enemata. Taking these two periods, therefore, as a starting-point, the diet was increased until (during period D) double as much proteid was given, nearly twice as much fat, and a considerable increase in the quantity of carbohydrates; the total number of calories being increased from 3105·96 to 5026·43.

The following table shows the extra quantity of nitrogen retained in the body on increasing the amount of nitrogen in the food.

TABLE 18.—*The Increased Quantity of Nitrogen retained in the body on increasing the amount given in the diet in Case* 1.

Period.	Increase of nitrogen ingested over previous diet, in grammes.	Increase or decrease of nitrogen excreted over previous periods, in grammes.[1]	Increased amount of nitrogen retained, in grammes.
A	—	—	+0·32
B	+ 3·42	−3·17	+6·59
C	+15·07	+6·84	+9·23
D	+ 6·18	+5·27	+0·91

It will be seen from the above that on the diet in period B, the retention of nitrogen was very satisfactory, while the quantity excreted was at its minimum. On the diet in period C, there was certainly a greatly increased retention of nitrogen in the body; but the extra quantity excreted amounted to nearly half the increased quantity of this substance ingested, and it was causing an over-strain on the intestinal tract, as has already been pointed out in discussing this period. Almost the whole of the extra nitrogen ingested in period D was immediately excreted, as there was only an extra 0·94 grammes retained in the body, although the increase in the quantity of food was no less than 6·21 grammes; and thus an excessive strain was thrown on the organism without attaining any appreciable result.

From these considerations, it appears that the diet given in period B was probably the maximum which could be advantageously made use of by the patient. This consisted of a slight excess of proteids (137·50 grammes), a moderately increased quantity of fats (136·96 grammes), and a somewhat small amount of carbohydrates (296·32 grammes), and would have been a very generous diet even if the patient had been up to weight, healthy, and at work.

[1] That found in both the urine and fæces.

TABLE 19.—*The proportion of the total Nitrogen in the Urine excreted as Urea, Uric Acid, and Ammonia in Case* 1.

Period.	Total nitrogen in urine.	Nitrogen as urea.	Nitrogen as uric acid.	Nitrogen as ammonia.	Nitrogen as nitrogen rest.
A ...	16·64 ...	85·71 ...	1·66 ...	1·42 ...	11·21
B ...	14·53 ...	87·92 ...	1·49 ...	1·51 ...	9·07
C ...	20·82 ...	79·89 ...	1·12 ...	0·81 ...	18·18
D ...	23·88 ...	79·33 ...	1·14 ...	1·32 ...	18·21

The averages of the Periods are here given.

From the foregoing table, it will be seen that the greatest percentage of nitrogen in the urine was excreted in the most oxydised form (urea) in the second Period (B), while in Periods C and A the quantity passed in this form diminished below the normal. Conversely, the quantity excreted as nitrogen rest doubled during Periods C and D, in comparison with that found in Period B. Thus, a very valuable indication is afforded as to when the strain on the organism of the body is becoming excessive.

The marked increase in the average quantity of ammonia excreted per diem in Period D is of interest, as it shows a sudden tendency in the organism to break down under over-strain.

The steady increase in the average quantity of sulphates excreted during periods C and D shows that the proteid metabolism was proceeding vigorously, but the marked rise in the average quantity of the aromatic sulphates also indicates that this metabolism was not proceeding at a sufficient rate to deal with the large quantity supplied, and that, consequently, the amount of intestinal putrefaction was increasing. This is also indicated by the diminution in the ratio between the alkaline and the aromatic sulphates, owing to the increase in the latter.

The marked rise in the average quantity of nitrogen excreted in the two latter periods—especially in period D—indicates the danger and uselessness of cramming

these patients to too great an excess. This is further brought out by the decline in the percentage absorbed, since, from the satisfactory figure (97·45 per cent.) in Period B, the percentage absorbed diminished to 89·95 in Period D. As has been already mentioned, no notice has been taken of the results in Period A in these considerations, owing to the administration of enemata.

The excretion of fats, although large, in Period D did not show such great variations as that of the nitrogen, and the lowest percentage obtained (that of Period D, 96·41) was still within the normal limits, so that these substances are of great value in the diet in this disease.

On turning to the consideration of the weight it will be seen that there was a gain in each period. The increase (1·58 kilos.) in period B was very satisfactory, and although the gain was more marked in Periods C and D, still, as has been before pointed out, the increase was obtained at too great a cost.

Clinically the state of the patient was most satisfactory during Periods A and B; but on increasing the diet in Periods C and D, the subjective symptoms —as already mentioned—increased to such an extent that it would have been impossible for him to have continued on either of these diets.

During the four weeks that the patient was under observation his pyrexia steadily diminished, and the condition of his lungs improved markedly, so that this method of treatment showed clinically that it was of advantage to the patient.

CASE 2.—*Pulmonary Tuberculosis—Moderately early stage, with considerable degree of arrest.*

Clinical History.—Age thirteen, schoolboy, admitted May 16th, 1900. This case was also an early one, being only of five months' duration. On admission he only weighed 31·05 kilos., and had a slight amount of fever. There was early infiltration of the left apex, with some

softening, and his sputum, which was small in amount (1 drachm) contained numerous tubercle bacilli.

On the commencement of the metabolism experiments three months later he was considerably improved in every respect, his general health being completely restored. He had been free from fever for several weeks, and had no cough or expectoration. His weight was 33·60 kilos. (without his clothes), so that he had gained 2·55 kilos. since admission. His physical signs now suggested the presence of a small dry cavity at the left apex. His appetite and digestion were excellent, and he was in the grounds all day taking a considerable amount of walking exercise.

TABLE 20.—*The various Diets and number of Calories given in Case 2, together with the percentage of Nitrogen and Fats absorbed, etc.*

	Period.			
	A	B	C	D
Proteids	147·88	145·19	160·38	156·81
Fats	212·48	192·46	179·83	166·11
Carbo-hydrates	222·25	217·04	271·45	314·44
Total calories	3567·82	3352·37	3442·92	3476·95
Calories per kilo.	105·87	97·17	104·15	102·92
Fluids	1854	2043	2586	2698
Nitrogen in urine	13·21	14·66	16·47	14·22
Urea	24·15	26·99	27·35	22·42
Nitrogen in fæces	0·96	0·89	1·00	1·07
Fat „	3·20	2·45	1·83	2·62
Nitrogen absorbed per cent.	95·88	96·29	96·11	95·76
Fat „ „	98·52	98·93	99·14	98·43
Weight at end of period	34·09	34·76	35·10	35·33

Period A.—During this period the patient was kept on the ordinary diet in use in the open-air wards at Brompton Hospital, and the daily average quantity of food taken by him was :—147·88 grammes of proteid, 212·48 grammes of fat, and 222·25 grammes of carbohydrates. It will be seen from the above that this diet contained a large quantity of fats, but the patient took it well, except on

the second day of analysis, when only 202·15 grammes of this substance were consumed. On the last day of analysis he only took 199·94 grammes of carbohydrates, as he did not finish the allotted quantity of bread. The total number of calories contained in this diet was 3567·82, and the average number of calories per kilo. body-weight during the analytical period was 105·87.

Though this is naturally a very large number of calories, it must be remembered that the patient was a growing boy, and was taking a good deal of exercise; and, as a rule, it did not cause him any discomfort. The quantity of fluids taken daily averaged 1854 c.c., principally due to the quantity of milk ordered.

The average quantity of nitrogen contained in the diet was 23·66 grammes and the total quantity found was 13·21 grammes in the urine, and 0·96 grammes in the fæces, so that 9·94 grammes were retained in the body.

The average quantity of urine excreted *per diem* was 1353 c.c., a quantity rather above the normal, considering the patient's age. But in this connection it must be remembered that he was taking a considerable quantity of fluid. The average specific gravity was 1015.[1]

TABLE 21.—*The Daily Excretion of Nitrogen and Nitrogenous Substances in the Urine in Case 2 on Diet II.*

Date.	Nitrogen.	Urea.	Uric acid.	Ammonia.
8— 9	15·48	28·91	0·37	0·33
9—10	8·64	14·69	0·20	0·30
10—11	12·43	23·44	0·39	0·22
11—12	16·28	29·56	0·60	0·28
Average	13·21	24·15	0·39	0·28

The average daily excretion of total nitrogen during the four days of analysis was 13·21 grammes, and this quantity was distributed amongst the nitrogen-containing

[1] Unfortunately the sp. gr. was not taken on the first day of analysis, so that the average only of the later days is given.

substances in the urine in the following manner :—84·04 per cent. was excreted in the form of urea, 0·94 per cent. in that of uric acid, and 1·80 per cent. in that of ammonia, so that 13·22 per cent. was excreted in the form of nitrogen rest.

The average daily excretion of urea was 24·15 grammes, that of uric acid 0·39 grammes, and that of ammonia 0·28 grammes, the quantity of the last-named constituent being rather above the normal.

TABLE 22.—*The Daily Excretion of Inorganic Substances in the Urine in Case 2 on Diet A.*

Date.	Phosphoric acid.	Chlorides.	Sulphates.			
			Total.	Alkaline.	Aromatic.	Ratio.
8— 9	2·48	9·73	3·02	2·89	0·13	23 :1
9—10	1·63	2·75	1·82	1·74	0·08	21·7:1
10—11	2·27	3·56	2·37	2·27	0·10	22·7:1
11—12	2·48	6·27	3·05	2·92	0·13	22·3:1
Average.	2·22	5·59	2·57	2·46	0·11	22·4:1

As regards the inorganic constituents of the urine, the average excretion of phosphoric acid was 2·22 grammes per diem and the elimination of this substance remained fairly constant, except on the second day of analysis, when only 1·63 grammes were passed. The excretion of the chlorides varied markedly, being 9·73 grammes on the first day of analysis and only 2·75 grammes on the following day. The average of the four days was, however, 5·59 grammes.

The average daily excretion of total sulphates in the urine was 2·57 grammes, so that proteid metabolism was not very active. Of this quantity 2·46 grammes represented the alkaline sulphates, so that the quantity of the aromatic sulphates excreted (0·11 grammes) was very low, and therefore the ratio of the alkaline to the aromatic sulphates was high, being 22·4 : 1.

TABLE 23.—*The Daily Excretion of Nitrogen and Fats in the Fæces in Case 2 on Diet A.*

Date.	Quantity.	Water per cent.	Nitrogen.	Fats.
8— 9	150	78·03	1·31	4·36
9—10	116	82·46	0·81	1·89
10—11	81	76·77	0·75	3·36
11—12	122	80·30	0·96	3·17
Average	117	79·39	0·96	3·20

On turning to the consideration of the fæces, it will be seen that the average quantity of nitrogen excreted in the fæces per diem was 0·96 grammes, a quantity much above the normal, and the same remark applies to the fats, which averaged 3·20 grammes.

TABLE 24.—*The Daily Diet and percentage of Nitrogen and Fats absorbed in Case 2 on Diet A.*

Date.	Nitrogen in diet.	Fats in diet.	Nitrogen absorbed per cent.	Fats absorbed per cent.
8— 9	24·14	215·59	94·57	97·98
9—10	23·10	202·15	96·49	99·07
10—11	23·16	215·84	96·76	98·44
11—12	22·24	216·33	95·68	98·58
Average	23·66	212·48	95·88	98·52

The daily average absorption of nitrogen was satisfactory, being 95·88 per cent., and a similar remark applies to the fats, as, on an average, 98·52 per cent. was absorbed.

The patient's weight on the last day of this period was 34·09 kilos., and the average weight for the four days of analysis 33·7 kilos.

Clinically the patient felt well, his appetite was good, and altogether he felt that he had been making progress during the week.

Period B.—It was intended to keep the patient on the same diet during this week, but, owing to one of the temporary diminutions in appetite, which is so common

in this disease, he did not take his food quite so well, especially on the last day. Therefore the average daily quantity taken was diminished, particularly in the case of the fats. The average quantity of proteids consumed was 145·19 grammes, of fats 192·46 grammes, and of carbohydrates 217·04 grammes. Principally owing to the lessened quantity of fats taken, the average total number of calories fell from 3567·82 to 3352·37. The number of calories per kilo. body-weight diminished from 105·87 to 97·17, but some of this decline was due to the increase in weight. Owing to the patient taking a larger quantity of water, the average of fluids consumed per diem rose to 2043 c.c.

The quantity of nitrogen contained in the diet averaged 23·23 grammes per diem, and since 14·66 grammes were found in the urine, and 0·89 gramme in the fæces, 7·68 grammes were retained in the body—that is, rather less than the quantity retained in the previous period (9·49 grammes).

Notwithstanding the increase in the average quantity of fluid taken per diem, the daily quantity of urine passed averaged only 1225 c.c., there being thus an average diminution of 128 c.c. per diem, as compared with that in period A. There was no change in the average specific gravity, which remained 1015.

TABLE 25.—*The Daily Excretion of Nitrogen and Nitrogenous Substances in the Urine in Case 2 on Diet B.*

Date.	Nitrogen.	Urea.	Uric acid.	Ammonia.
15—16	16·12	28·18	0·39	—
16—17	12·65	24·19	0·36	0·24
17—18	13·62	26·32	0·56	0·29
18—19	16 23	29·25	0·56	0·20
Average	14·66	26·99	0·47	0·24

The average daily excretion of nitrogen in the urine increased from 13·21 grammes in period A to 14·66 grammes during this week, and this quantity was distributed amongst the nitrogen-containing constituents

of the urine as follows :—86·28 per cent. was excreted in the form of urea, that is to say, a slightly increased percentage over that of the previous period. There was also a slightly increased amount excreted in the form of uric acid, the quantity in this period amounting to 1·07 per cent.; but the quantity excreted in the form of ammonia diminished to 1·44 per cent. The average quantity excreted in the form of nitrogen rest was 11·21 per cent., and was therefore slightly below that of period A, when 13·22 per cent. was excreted.

The average daily quantity of urea excreted was 26·99 grammes, and that of uric acid 0·47 gramme, both of these substances showing a slight increase over period A. The quantity of ammonia excreted averaged 0·24 gramme *per diem*—a slight decrease as compared with that in the previous period.

TABLE 26.—*The Daily Excretion of the Inorganic Substances in the Urine in Case* 2 *on Diet B.*

Date.	Phosphoric acid.	Chlorides.	Sulphates.			
			Total.	Alkaline.	Aromatic.	Ratio.
15—16 .	2·71 ...	5·29 ...	2·81 ...	2·68 ...	0·13 ...	22·2 : 1
16—17 .	2·20 ...	4·95 ...	2·67 ...	2·60 ...	0·07 ...	37·1 : 1
17—18 .	2·36 ...	3·29 ...	2·51 ...	2·39 ...	0·12 ...	19·9 : 1
18—19 .	2·70 ..	3·39 ...	2·38 ...	2·25 ...	0·13 ...	17·3 : 1
Average .	2·49 ...	4·23 ...	2·59 ...	2·48 ...	0·11 ...	22·5 : 1

On turning to the consideration of the inorganic substances in the urine, it is to be noticed that there was a slight rise in the average excretion of phosphoric acid, as 2·49 grammes were passed as compared with 2·22 grammes in period A. There was a considerable fall in the average daily excretion of chlorides, 4·23 grammes being eliminated as compared with 5·59 grammes in the previous period, this decrease being much more than could be accounted for by the slight diminution in the diet. There was practically no change in the average excretion of total sulphates in the urine (2·59 grammes) as compared with period A, and of this amount 2·48

grammes were passed in the form of alkaline sulphates, so that the excretion of aromatic sulphates still remained at the previous low level (0·11 gramme). From this it is seen that the ratio of the alkaline to the aromatic sulphates was 22·5 : 1, that is, the same as in the previous period.

TABLE 27.—*The Daily Excretion of Nitrogen and Fats in the Fæces in Case 2 on Diet B.*

Date.	Quantity.	Water per cent.	Nitrogen.	Fats.
15—16	108	77·20	1·04	2·68
16—17	128	80·00	1·07	2·86
17—18	83	78·18	0·76	2·04
18—19	89	81·77	0·78	1·81
Average	102	79·29	0·89	2·45

On turning to the consideration of the fæces, it will be seen that the quantity of nitrogen excreted in this manner was practically the same as in period A, since 0·89 gramme were passed on an average *per diem* during this week, and this notwithstanding the fact that there was a slight diminution in the quantity of nitrogen given in the food. The average daily excretion of fats in the fæces also showed a slight diminution, from 3·20 grammes to 2·45 grammes, and this quantity is, if anything, rather below that found in normal individuals, who are taking an ordinary amount of fat in the diet, and is, therefore, very small in comparison with the large quantity of fats ingested.

TABLE 28.—*The Daily Diet and Percentage of Nitrogen and Fats absorbed in Case 2 on Diet B.*

Date.	Nitrogen in diet.	Fats in diet.	Nitrogen absorbed per cent.	Fats absorbed per cent.
15—16	24·76	203·18	95·79	98·68
16—17	23·57	219·57	95·42	96·61
17—18	22·67	240·53	96·65	99·45
18—19	21·92	173·79	96·89	98·96
Average	23·23	192·46	96·29	98·93

Notwithstanding the slight decrease in the quantity of proteid given in the food, there was a slight rise in the rate of absorption of nitrogen, as 96·29 per cent. was absorbed on an average each day. The average quantity of fats absorbed increased very slightly, and reached the high rate of 98·93 per cent. There was therefore a very excellent utilisation of these constituents of the diet, and the slight diminution in the quantities given in the food was, if anything, of benefit.

The weight on the last day of this period was 34·76 kilos.—a gain of 0·67 kilo. over the corresponding day of period A, while the average on the four days on which analyses were carried out was 34·5 kilos.—a gain of 0·8 kilo. over the corresponding period.

Clinically the patient felt extremely well, and though the average quantity of food taken was slightly smaller, he did not feel himself that his appetite was not as good as in the previous period.

Period C.—As we have now obtained two practically normal periods—that is to say, normal periods in respect of the diet that the patient had been on during the previous three months—it was decided to increase the quantity of proteids and carbohydrates, while further slightly diminishing the amount of the fats. The patient took his food well, except on the second day of analysis, when the quantity of carbohydrates consumed was low (254·17 grammes). In comparison with the other days the average daily quantity of proteids in the diet was 160·38 grammes—an increase of 15·19 grammes over that given in period B. The quantity of the fats was diminished by 12·63 grammes, so that the average taken *per diem* during this week was 179·83 grammes, while the average amount of the carbohydrates was increased by 54·41 grammes, so that the total quantity taken each day was 271·45 grammes. The total number of calories contained in this diet was 3442·92—a slightly greater number than in period A, as the increase caused by the larger amount of carbohydrates given was partly neutralised by

the diminution in the quantity of fats ingested. The average number of calories per kilo. body-weight was 104·15. Owing to the increased quantity of milk given, the average amount of fluid consumed each day rose to 2586 c.c.

There was an average of 25·66 grammes of nitrogen contained in the daily diet, and 16·47 grammes of this substance were found in the urine, and 1·00 gramme in the fæces, so that 8·19 grammes were retained in the body, this being practically equal to the retention in period B, notwithstanding the fact that 2·43 grammes more nitrogen were given in the food.

The average daily excretion of urine rose considerably, being 1685 c.c. as against 1225 c.c. in period B, and this increase was almost proportional with the increased quantity of fluids given. The average specific gravity decreased to 1012, evidently owing to the larger quantity of water passed, as, on referring to the tables, it is seen that the average amounts of all the substances analysed for showed an increase.

TABLE 29.—*The Daily Excretion of Nitrogen and Nitrogenous Substances in the Urine in Case* 2 *on Diet C.*

Date.	Nitrogen.	Urea.	Uric acid.	Ammonia.
22—23 .	17·61 ...	26·38 ...	0·35 ...	0·37
23—24 .	15·66 ...	25·39 ...	0·47 ...	0·20
24—25 .	14·26 ...	26·68 ...	0·42 ...	0·22
25—26 .	18·35 ...	30·96 ...	0·64 ...	0·54
Average	16·47 ...	27·35 ...	0·47 ...	0·33

The average excretion of total nitrogen *per diem* in the urine increased to 16·47 grammes as compared with 14·66 grammes in the previous period. The distribution of the nitrogen amongst the nitrogen-containing constituents of the urine was such that 77·97 per cent. was excreted in the form of urea—a decided decrease on the 86·33 per cent. found in this form in period B; 0·95 per cent. was eliminated in the form of uric acid,

while the amount excreted in the form of ammonia was 1·62 per cent. There was consequently a marked rise in the amount of nitrogen excreted in the form of nitrogen rest, 19·41 per cent. being eliminated in this form as against 11·16 per cent. in the previous period. Taken in conjunction with the diminished percentage excreted in the form of urea, this large quantity suggests that the liver was becoming unable to perform its functions properly.

The average daily quantity of urea excreted rose slightly to 27·35 grammes, that of uric acid remained the same, 0·47 gramme, while there was a slight increase in that of ammonia, 0·33 gramme.

TABLE 30.—*The Daily Excretion of the Inorganic Substances in the Urine in Case* 2 *on Diet C.*

Date.	Phosphoric acid.	Chlorides.	Sulphates.			
			Total.	Alkaline.	Aromatic.	Ratio.
22—23	2·83	7·44	3·02	2·88	0·14	20·3 : 1
23—24	2·56	5·37	2·82	2·67	0·15	17·8 : 1
24—25	2·53	5·29	2·83	2·69	0·14	19·2 : 1
25—26	2·57	6·24	3·42	3·25	0·17	18·6 : 1
Average	2·62	6·09	3·02	2·87	0·15	19·1 : 1

Having considered the behaviour of the nitrogen-containing bodies in the urine, we now turn to the inorganic substances analysed for, and, taking the phosphoric acid first, it will be noticed that there was a further slight rise in this substance (2·62 grammes being the average daily excretion as compared with 2·49 grammes in the previous period). As has been pointed out in discussing period C of Case 1, the average daily excretion of the chlorides showed a considerable increase on increasing the diet, 6·09 grammes being eliminated as compared with 4·23 grammes in period B. The average daily quantity of total sulphates excreted in the urine increased to 3·02 grammes, so that there was an increase in the proteid metabolism, and 2·87

grammes of this amount was excreted in the form of alkaline sulphates, so that the average of the aromatic group *per diem* increased to 0·15 gramme. From this it will be seen that the ratio of the alkaline to the aromatic sulphates diminished slightly, being 19·1 : 1.

TABLE 31.—*The Daily Excretion of Nitrogen and Fats in the Fæces in Case* 2 *on Diet C.*

Date.	Quantity.	Water per cent.	Nitrogen.	Fats.
22—23	130	76·85	1·36	2·46
23—24	128	83·81	0·93	1·69
24—25	123	81·85	1·01	1·92
25—26	137	88·71	0·70	1·26
Average	130	82·81	1·00	1·83

The average daily quantity of nitrogen excreted in the fæces show a slight rise, being 1·00 gramme as compared with 0·89 gramme in the previous period; but this quantity is well within the normal limits. The average quantity of fats excreted per diem in the fæces was very low, being only 1·83 grammes, and shows that the intestinal tract was able to deal more satisfactorily with the quantities given in the diet.

TABLE 32.—*The Daily Diet and Percentage of Nitrogen and Fats absorbed in Case* 2 *on Diet C.*

Date.	Nitrogen in diet.	Fats in diet.	Nitrogen absorbed per cent.	Fats absorbed per cent.
22—23	26·06	186·09	94·78	98·68
23—24	25·70	169·27	96·38	99·00
24—25	25·89	193·63	96·09	98·96
25—26	24·92	167·13	97·19	99·91
Average	25·66	179·83	96·11	99·14

There was practically no change in the percentage of nitrogen absorbed, the average daily amount in this period being 96·11 per cent., so that the total quantity of nitrogen absorbed was greater than in period B, as

the quantity given in the food had been increased in this period. 99·14 per cent. of fats were absorbed, this being practically the maximum absorption that has been found in any metabolism experiments that we are acquainted with.

The weight on the last day of this period was 35·10 kilos. Therefore the gain on the corresponding day of period B was very slight, being only 0·36 kilo. The average weight on the four days of analyses was 35·0 kilos., so that there was an increase of 0·5 kilo. over that of the previous week.

Clinically the patient felt extremely well throughout the week, except on the last day, when there was a slight attack of vomiting. This, however, did not at all interfere with his appetite, which remained good, and did not diminish at the commencement of the following period.

Period D.—Notwithstanding the attack of vomiting previously alluded to, it was decided to increase the quantity of carbohydrates in this period, while further diminishing that of the fats. The original intention was to keep the quantity of proteids the same, but unfortunately the patient did not take his proteid food quite so well. However, as the average daily quantity consumed was 156·81 grammes, the diminution was extremely slight, being less than 3 grammes per diem. On the last two days of the analytical period there was a marked decrease in the quantity of the fats taken, so that the daily average only worked out at 166·11 grammes, and a similar state of things occurred in the case of the carbohydrates, the average here being 314·44 grammes. The total number of calories contained in this diet was 3476·95, as the lessened number of calories taken in the form of fats was almost entirely neutralised by the larger number taken in the form of carbohydrates, so that there was practically no difference between the total number of calories in this period as compared with that contained in the diet in period C. Owing to a

slight increase in weight the number of calories per kilo. body-weight diminished very slightly, being 102·92. The average quantity of fluids consumed each day was slightly increased, being 2698 c.c.

The amount of nitrogen contained in the average daily quantity of proteid taken was 25·09 grammes, and since 14·22 grammes of this substance were found in the urine, and 1·07 grammes in the fæces, 9·80 grammes were retained in the body—rather more than that retained in periods B and C, but only slightly in excess of that in period A. The average quantity of urine excreted per diem diminished to 1435 c.c., despite the fact that the quantity of fluids taken was slightly increased during this period, while the specific gravity remained the same, 1012.

TABLE 33.—*The Daily Excretion of Nitrogen and Nitrogenous Substances in the Urine in Case 2 on Diet D.*

Date.	Nitrogen.	Urea.	Uric acid.	Ammonia.
29—30 .	14·13 ...	22·73 ...	0·49 ...	0·42
30—31 .	11·10 ...	16·41 ...	0·46 ...	0·27
31— 1 .	13·92 ...	19·49 ..	0·50 ...	0·53
1— 2 .	18·63 ...	31·05 ...	0·64 ...	0·62
Average .	14·22 ...	22·42 ...	0·52 ...	0·46

The excretion of total nitrogen in the urine averaged 14·22 grammes per diem—a considerable decrease from the 16·47 grammes found during period C. The amount of nitrogen excreted in the form of urea was only 71·79 per cent., there being thus a considerable further diminution in the amount excreted in this form, as compared with period C, when 77·97 per cent. of nitrogen was eliminated in the form of urea.

The amount eliminated in the form of uric acid was slightly increased (1·23 per cent.), while there was a marked rise in the amount excreted in the form of ammonia, 2·59 per cent. being eliminated in this manner,

as against 1·62 per cent. in the previous period. In this period the amount of nitrogen excreted in the form of nitrogen rest was extremely high, and was nearly one quarter of the total excretion, since 24·41 per cent. was eliminated in this manner. This, taken in conjunction with the low percentage of nitrogen eliminated in the form of urea, and also with the increase in that found in the form of ammonia, is a very strong indication that the elaboration and oxidisation of proteids were being seriously impaired. The average daily excretion of urea diminished to 22·42 grammes, that of uric acid increased slightly to 0·52 gramme. The average daily excretion of ammonia rose from 0·33 gramme to 0·46 gramme, this considerable increase pointing to commencing diminished alkalinity of the blood.

TABLE 34.—*The Daily Excretion of the Inorganic Substances in the Urine in Case* 2 *on Diet D.*

Date.	Phosphoric acid.	Chlorides.	Sulphates. Total.	Alkaline.	Aromatic.	Ratio.
29—30	2·18	3·39	2·42	2·31	0·11	21 : 1
30—31	1·73	3·64	2·04	1·95	0·09	21·7 : 1
31— 1	1·98	2·78	2·44	2·35	0·09	26·1 : 1
1— 2	3·20	7·66	3·13	2·98	0·15	19·1 : 1
Average	2·27	4·37	2·51	2·40	0·11	21·8 : 1

In common with the other inorganic constituents of the urine there was a decided diminution in the quantity of phosphoric acid excreted per diem, 2·27 grammes only being found as compared with 2·62 grammes in the previous period. The decrease in the quantity of chlorides excreted was marked, the daily average being only 4·37 grammes as compared with 6·09 grammes in period C, notwithstanding the fact that the diet remained practically the same.

The average daily excretion of the total sulphates in the urine diminished to 2·51 grammes, that is practically the same as in the first two periods, so that there was a

decrease in the proteid metabolism. 2·40 grammes of this quantity were eliminated in the form of alkaline sulphates, so that the quantity eliminated in the aromatic group fell again to its original amount, that is 0·11 gramme. There was, consequently, a slight increase in the ratio of the alkaline to the aromatic sulphates, which worked out in this period to 21·8 : 1.

TABLE 35.—*The Daily Excretion of Nitrogen and Fats in the Fæces in Case 2 on Diet D.*

Date.	Quantity.	Water per cent.	Nitrogen.	Fats.
29—30	144	79·97	1·32	3·21
30—31	140	82·74	1·11	2·80
31— 1	98	79·23	0·94	2·26
1— 2	114	82·68	0·91	2·20
Average	124	81·16	1·07	2·62

On turning to the consideration of the fæces it will be seen that the quantity of nitrogen excreted in this manner rose again slightly to 1·07 grammes, as compared with 1·00 gramme in period C, the former figure still being within the normal limits of excretion of this substance. Notwithstanding the fact that there was a further diminution in the quantity of fats ingested, the average daily excretion of this substance increased slightly, being 2·62 grammes as compared with 1·83 grammes in period C.

TABLE 36.—*The Daily Diet and Percentage of Nitrogen and Fats absorbed in Case 2 on Diet D.*

Date.	Nitrogen in diet.	Fats in diet.	Nitrogen absorbed per cent.	Fats absorbed per cent.
29—30	25·79	184·66	94·88	98·26
30—31	25·48	184·42	95·64	98·48
31— 1	24·14	156·01	96·19	98·55
1— 2	24·43	139·26	96·32	98·42
Average	25·09	166·11	95·75	98·43

On account of the slightly lessened quantity of nitrogen taken in the food, and the rather larger amount found in the fæces, the absorption of this substance diminished to 95·75 per cent., and though rather below the normal limits, still remained at a fairly high level. 98·43 per cent. of the fats given in the diet were absorbed, so that the rate of absorption of this substance remained extremely good all through.

On the last day of this period the patient weighed 35·33 kilos., so that the gain since the corresponding day of period C was very small, being only 0·23 kilo. On taking the average of the four days of analysis in this period, there was a gain of 0·4 kilo. over the previous period, the average weight being 34·4 kilos.

From a clinical standpoint the patient was getting on well and his appetite remained good. He did not feel, however, as if he could have continued very much longer on this diet, though unable to give us any satisfactory reason why not, and he did not complain of any symptoms indicative of digestive troubles.

Summary.—At the commencement of the time that this patient was under observation he was still somewhat below his proper weight; his condition in every other respect was satisfactory.

As has already been mentioned, the patient was kept, during the first two periods, on the diet that he had been taking since his admission to the hospital, so as to obtain an idea of his ordinary metabolism during his stay in the hospital. It will be noticed, however, that the usual hospital diet was too much for this patient, as on weighing his food we discovered that on no day did he take the full quantity sent up to him. Having thus obtained an idea of his metabolism, it was decided to try the effect of slightly increasing the quantity of proteids, at the same time making a progressive increase in the amount of carbohydrates, while the quantity of the fats was gradually diminished. On account of the higher caloric value of fat-containing foods the total number of calories was

at the maximum in period A and at the minimum in period B; as in this latter period the quantity of carbohydrates had not been increased sufficiently to make up for the diminution caused by the higher caloric value of the fat-containing foods. In periods C and D the number of calories approximated closely with that of the first period; as in these periods the quantity of carbohydrates was almost sufficient to neutralise the diminished amount of fats given from the caloric standpoint. On account of the increase in weight the number of calories per kilo. body-weight diminished slightly in the later periods, but remained at a very high level all through.

The following table shows the different quantities of nitrogen retained in the body on varying the amounts of the diet.

TABLE 37.—*The Increased or Decreased Quantity of Nitrogen on increasing or decreasing the Amount given in the Diet in Case* 2.

Period.	Increase or decrease in nitrogen ingested over previous period, in grammes.	Increase or decrease in nitrogen excreted over previous period, in grammes.[1]	Increase or decrease in amount of nitrogen retained, in grammes.
A ...	— ...	— ...	+9·49
B ...	−0·43 ...	+1·38 ...	−1·81
C ...	+2·43 ...	+1·92 ...	+0·51
D ...	−0·57 ...	−2·18 ...	+1·61

It will be seen from the above that, considering the quantities of proteids given in the foods, the best absorption was obtained in period A. The quantity absorbed in period D was very slightly better, but, as will be seen on referring to the clinical remarks at the end of this period, the patient was unable to continue this diet for long. In period C practically the whole of the extra nitrogen ingested was immediately excreted, while in period B there was an increased excretion as well as a decreased ingestion.

As will be seen later, the increased retention in period

[1] That found in both urine and fæces.

D was accompanied by a very large increase in the quantity of nitrogen excreted as nitrogen rest—that is, nitrogen excreted in a less oxidised form, and therefore the results obtained on this diet were at too great a cost in the efficiency of the organism.

On the whole, the diet in period A appears to be the most satisfactory for this patient, it being a very generous one for a growing boy of his age. To recapitulate, it consisted of 147·8 grammes proteids, 212·48 grammes fats, and 222·25 grammes carbohydrates; and therefore contained a slight excess of proteids, a considerable excess of fats, and a slightly diminished quantity of carbohydrates.

TABLE 38.—*The Proportion of the Total Nitrogen in the Urine excreted as Urea, Uric Acid, and Ammonia in Case 2.*

Period.	Total nitrogen in urine.	Nitrogen as urea.	Nitrogen as uric acid.	Nitrogen as ammonia.	Nitrogen as nitrogen rest.
A ...	13·21	83·04	0·94	1·80	14·22
B ...	14·66	86·33	1·07	1·44	11·16
C ...	16·47	77·97	0·95	1·62	19·41
D ...	14·22	71·79	1·23	2·59	24·41

The averages of the Periods are here given.

The quantity of nitrogen excreted in the most highly oxidised form (urea) is seen from the above to be greatest in Period B, although fairly good in Period A. The effect of increasing the strain on the organism by increasing the diet—especially in carbohydrates—is well shown in Periods C and D, as in addition to the marked diminution in the percentage of nitrogen excreted in the form of urea, there was a marked increase in that excreted as nitrogen rest; the latter rising, in the last Period, to the very high amount of 24·41 per cent., thus showing that the metabolic organs were unable to bear the strain.

The marked increase in the quantity of ammonia excreted per diem in period D, and the large quantity

eliminated (0·46 gramme), also indicated an excessive strain on the organism and showed that there was certainly a tendency to diminishing the alkalinity of the blood.

The excretion of sulphates in the urine indicated that, considering the patient's age, the proteid metabolism was proceeding actively, and the small amounts passed in the aromatic group show that there was no excess of intestinal putrefaction going on in any of the Periods.

The average quantity of nitrogen excreted in the fæces remained within the normal limits throughout. The absorption of this substance was within the lower normal limits all through, although in the last period it was, if anything, slightly below them.

The average excretion of fats was low, especially in Period C, when it only amounted to 1·83 grammes, and, consequently, the absorption was very good all through, the rate obtained (99·14 per cent.) in Period C being extremely high. These absorption rates point out the desirability of including large quantities of fats in the dietary of phthisical patients.

Clinically the patient felt very well throughout the first two Periods, but the attack of vomiting on the last day of Period C appears to have been an indication that the highest point in "cramming" had been reached, and, as already mentioned, he felt at the end of Period D that he could not have continued on the larger diet.

The gain in weight was satisfactory, as, in the four weeks that he was under observation, it amounted, on taking the averages of the Periods, to 1·7 kilos.

The report on the condition of his lesion at the conclusion of the experiment was very satisfactory, as it showed that it was almost completely quiescent.

Case 3.—*Tubercular chronic pulmonary infiltration and softening* (*fairly limited*) *with considerable arrest.*

Clinical history.—Age twenty-one, carman, admitted April 23rd, 1900. Physical state—right lung, infiltra-

tion and softening of apex of upper lobe; left lung, infiltration of both lobes. He had a high degree of fever and much constitutional disturbance, and his weight at this time was 61·65 kilos., his greatest known weight having been 73·35 kilos. (in his clothes).

On August 8th, after three months' treatment, he was much better, and was practically apyrexical.

His physical signs showed a considerable degree of arrest in the progress of the disease, and he had gained 6·08 kilos., so that he was nearly up to his normal weight. He was taking no exercise, his appetite was beginning to fail, and he had recently had a good deal of dyspeptic trouble.

TABLE 39.—*The various Diets and Number of Calories given in Case* 3, *together with the Percentage of Nitrogen and Fats absorbed, etc.*

Period.	A.	B.	C.	D.
Proteids	144·31	143·00	169·31	167·18
Fats	211·82	183·03	203·42	162·87
Carbohydrates . . .	235·39	211·87	283·28	317·76
Total calories . . .	3526·70	3265·15	3747·13	3482·49
Calories per kilo. . .	54·01	49·62	34·85	31·21
Fluids	1854	1966	2474	2726
Nitrogen in urine . .	15·68	17·66	24·37	22·87
Urea	28·34	30·97	43·84	39·87
Nitrogen in fæces . .	1·11	0·96	1·59	1·90
Fat in fæces . . .	5·60	3·16	7·11	6·74
Nitrogen absorbed per cent.	95·09	95·79	94·06	92·66
Fat absorbed per cent. .	97·35	98·28	96·44	95·53
Weight at end of period .	65·36	66·26	66·83	67·05

Period A.—As has already been mentioned in the clinical account of this case, the condition of the patient was not very satisfactory at the commencement of this period; and, although he was nominally on the diet given in the open-air wards at Brompton Hospital, the average daily quantity taken during the four days of analysis was—144·31 grammes proteids; 211·82 grammes fat; 235·39 grammes carbohydrates, as he was in the

habit of leaving a considerable quantity of food each day. The average total number of calories contained in the diet consumed was 3526·70, and the number per kilo. body-weight 54·01. The average daily amount of fluids consumed was 1854 c.c.

The average quantity of nitrogen contained in this diet per diem was 23·09 grammes, and 15·68 grammes of this substance were excreted in the urine, and 1·11 grammes in the fæces. Therefore 5·30 grammes were retained in the body.

The average daily excretion of urine was very small, when the quantity of fluids taken is remembered, and was only 1055 c.c., the average specific gravity being rather high, 1021.

TABLE 40.—*The Daily Excretion of Nitrogen and Nitrogenous Substances in the Urine in Case* 3 *on Diet A.*

Date.	Nitrogen.	Urea.	Uric acid.	Ammonia.
8— 9 .	18·15 ...	32·40 ...	0·75 ...	0·32
9—10 .	15·82 ...	28·60 ...	0·88 ...	0·22
10—11 .	12·24 ...	22·88 ...	1·28 ...	0·13
11—12 .	16·52 ...	29·49 ...	0·90 ...	0·18
Average .	15·68 ...	28·34 ...	0·95 ...	0·22

The excretion of total nitrogen in the urine averaged 15·68 grammes per diem, and, of this amount, 84·56 per cent. was excreted in the form of urea and 2·15 per cent. in that of uric acid, 1·11 per cent. being eliminated in the form of ammonia, so that the quantity excreted in the form of nitrogen rest was 12·19 per cent.

The average quantity of urea excreted per diem was 28·34 grammes, that of uric acid 0·95 gramme, and that of ammonia 0·22 gramme.

TABLE 41.—*The Daily Excretion of the Inorganic Substances in the Urine in Case* 3 *on Diet A.*

Date.	Phosphoric acid.	Chlorides.	Sulphates.			
			Total.	Alkaline.	Aromatic.	Ratio.
8— 9	2·38	6·01	3·36	3·19	0·17	18·7 : 1
9—10	2·38	5·75	2·94	2·77	0·17	16·3 : 1
10—11	1·73	3·96	2·37	2·15	0·24	8·9 : 1
11—12	2·16	6·84	2·78	2·62	0·16	16·3 : 1
Average	2·16	5·64	2·87	2·68	0·19	14·1 : 1

On turning to the consideration of the inorganic substances analysed in the urine it will be seen that the average daily excretion of phosphoric acid was 2·16 grammes, that is, an amount slightly below the normal. The excretion of chlorides averaged 5·64 grammes per diem—a normal quantity considering the diet. The quantity of total sulphates excreted in the urine showed a daily average of 2·87 grammes, and, of this quantity, 2·68 grammes were passed in the form of alkaline sulphates, and 0·19 gramme in that of the aromatic group, this latter number being slightly below the normal. The ratio of the alkaline to the aromatic sulphates was 14·1 : 1.

TABLE 42.—*The Daily Excretion of Nitrogen and Fats in the Fæces in Case* 3 *on Diet A.*

Date.	Quantity.	Water per cent.	Nitrogen.	Fats.
8— 9	120	76·08	1·05	5·60
9—10	219	83·74	1·68	7·95
10—11	110	79·20	0·85	4·43
11—12	110	79·20	0·85	4·43
Average	140	79·67	1·11	5·60

It will be seen from the above table that the daily average excretion of nitrogen in the fæces was within the normal limits, being 1·11 grammes. The excretion of the fats was rather above the normal, but was not

high considering the large quantity taken in the diet, the daily average being 5·60 grammes.

TABLE 43.—*The Daily Diet and Percentage of Nitrogen and Fats absorbed in Case* 3 *on Diet A.*

Date.	Nitrogen in diet.	Fats in diet.	Nitrogen absorbed per cent.	Fats absorbed per cent.
8— 9 .	24·72 ...	221·92 ...	95·75 ...	97·48
9—10 .	20·66 ...	206·49 ...	91·87 ...	96·15
10—11 .	24·24 ...	221·71 ...	96·49 ...	98·02
11—12 .	22·74 ...	197·14 ...	96·26 ...	97·75
Average	23·09 ...	211·82 ...	95·09 ...	97·35

Considering the quantity of nitrogen given in the diet, and that found in the fæces, the rate of absorption (95·09 per cent.) was rather below that which would have been expected from a cursory glance, this amount being rather below the lower normal limits of absorption of this substance. On the other hand, the rate of absorption of the fats was satisfactory, being 97·35 per cent., and was normal considering the large quantity of fats given in the diet.

On the last day of this period the patient weighed 65·36 kilos., and the average weight for the four days during which analysis was carried out was 65·3 kilos., his weight having been stationary for some time.

Clinically the report for this week was that the patient took his food very well, although his appetite was failing and some dyspeptic symptoms were present. In addition, he was complaining of feeling drowsy and heavy.

Period B.—Owing to the condition not having been very satisfactory during the previous week, it was decided to keep him on the same diet. However, his appetite failed still more, and consequently the average daily quantity of food taken rather diminished, especially in the fats and carbohydrates, and the following was the absolute diet taken in this period:—143·00 grammes

fats, 183·03 grammes fats (that is, a decrease of 28·78 grammes), and 211·87 grammes of carbohydrates (a diminution of 23·52 grammes). The average total number of calories contained in this diet was 3265·15—a decrease of 261·24 as compared with that of period A. The average number of calories per kilo. body-weight was 49·62 as compared with 54·01 in the previous period. There was a slight increase in the average quantity of fluid taken per diem, as 1966 c.c. were consumed in this period as against 1854 c.c. in period A.

22·88 grammes of nitrogen were contained in the above diet, and 17·66 grammes of this substance were found in the urine, and 0·96 gramme in the fæces, so that 4·26 grammes were retained in the body—a slight decrease as compared with that found in the previous period, when 5·30 grammes were retained.

On the third day of analysis the quantity of urine excreted was very low, being only 400 c.c., but it was necessary to consider this amount as the total, as, on very careful investigation, we could find no evidence of any of the urine having been lost. On the succeeding day there was a very great increase in the quantity, 1675 c.c. being passed, and there had been very little storing up of solids during the preceding day, as the specific gravity was 1022.

The average excretion of urine for the four days was 1101 c.c., that is, slightly more than in the previous period, but still very low in comparison with the quantity of fluids taken. The average specific gravity was 1022.

TABLE 44.—*The Daily Excretion of Nitrogen and Nitrogenous Substances in the Urine in Case* 3 *on Diet B.*

Date.	Nitrogen.	Urea.	Uric acid.	Ammonia.
15—16 .	19·04 ...	33·10 ...	0·84 ...	0·28
16—17 .	16·00 ...	30·78 ...	0·86 ...	0·14
17—18 .	7·64 ...	15·08 ...	0·85 ...	0·24
18—19 .	27·97 ...	44·90 ...	1·22 ...	0·14
Average.	17·66 ...	30·97 ...	0·94 ...	0·20

The average excretion of total nitrogen in the urine per diem was 17·66 grammes, as against 15·68 grammes in period A. It should be mentioned that the quantity of nitrogen found on the third day of analysis was very small—7·64 grammes; but this was counterbalanced by the large quantity passed on the following day, 27·97 grammes, and supports the suggestion already made in considering the large quantity of urine passed on the former day. The distribution of the nitrogen amongst the various nitrogen-containing constituents in the body was as follows:—84·52 per cent. was eliminated in the form of urea, that is, practically, the same as in the former period; 2·01 per cent. was eliminated in the form of uric acid, and 1·24 per cent. in that of ammonia. The quantity of nitrogen excreted as nitrogen rest was 12·20 per cent, that is, practically, the same as in period A. The daily average excretion of urea was 30·97 grammes, the diminution on the third day of analysis being proportionate to the small quantity of nitrogen already mentioned. The excretion of uric acid, however, did not diminish on the third day of analysis in common with the other nitrogenous constituents, and the daily average was 0·94 gramme. The quantity of ammonia excreted on the third day of analysis was, comparatively speaking, larger, being 0·24 gramme, and the average per diem of this substance passed was 0·20 gramme.

TABLE 45.—*The Daily Excretion of the Inorganic Substances in the Urine in Case 3 on Diet B.*

Date.	Phosphoric acid.	Chlorides.	Sulphates.			
			Total.	Alkaline.	Aromatic.	Ratio.
15—16	3·08	2·35	2·99	2·79	0·20	13·1 : 1
16—17	2·07	6·32	2·38	2·21	0·17	12·1 : 1
17—18	0·88	2·56	1·25	1·18	0·07	17·1 : 1
18—19	4·19	7·37	4·94	4·70	0·24	19·6 : 1
Average	2·56	4·65	2·89	2·72	0·17	16·1 : 1

It will be seen from the above table that there was a rise in the average daily excretion of phosphoric acid, 2·56 grammes being eliminated in this period, as compared with 2·16 grammes in period A; while, on the contrary, the average daily excretion of the chlorides diminished from 5·64 grammes to 4·65 grammes. The quantity of total sulphates excreted in the urine was about the same as in the previous period, the daily average being 2·89 grammes. The alkaline sulphates represented 2·72 grammes of this amount, so that there was a slight diminution in the quantity of aromatic sulphates passed, 0·17 gramme, as compared with 0·19 gramme in period A. The ratio (16·1 : 1) of the alkaline to the aromatic sulphates consequently showed a slight increase.

TABLE 46.—*The Daily Excretion of Nitrogen and Fats in the Fæces in Case* 3 *on Diet B.*

Date.	Quantity.	Water per cent.	Nitrogen.	Fats.
15—16	130	80·00	1·04	3·42
16—17	149	79·22	1·23	4·07
17—18	102	81·16	0·77	2·54
18—19	103	81·16	0·78	2·62
Average	121	80·13	0·96	3·16

On turning to the consideration of the fæces, it will be seen that there was a slight diminution in the average daily quantity of nitrogen excreted in this manner, the quantity being 0·96 gramme as compared with 1·11 gramme in the previous period. While only this trifling diminution in the quantity of nitrogen was found, there was a decided decrease in the quantity of fats excreted, the daily average amount falling from 5·60 grammes to 3·16 grammes.

TABLE 47.—*The Daily Diet and Percentage of Nitrogen and Fats absorbed in Case 3 on Diet B.*

Date.	Nitrogen in diet.	Fats in diet.	Nitrogen absorbed per cent.	Fats absorbed per cent.
15—16	20·92	168·55	95·03	97·97
16—17	23·59	190·23	94·78	97·85
17—18	22·40	183·29	96·51	98·67
18—19	24·59	190·01	96·83	98·62
Average	22·88	183·03	95·79	98·28

Although there was a very slightly diminished quantity of nitrogen given in the food, the amount absorbed rose to 95·79 per cent., consequent on the lessened excretion of this substance in the fæces, so that the patient made use of practically the same amount of nitrogen as in the previous period. Despite the diminution on the quantity of fats given, the absorption rate reached the very satisfactory level of 98·28 per cent., and compares favourably with the 97·35 per cent. found in period A.

On the last day of this period the patient's weight was 66·26 kilos., so that there was a gain of 0·90 kilo. on that of the corresponding day of the previous week, while the average weight of the four days during which analyses were carried out was 65·8 kilos., there being thus only an improvement of 0·5 kilo. on comparing the two analytical periods.

The clinical note at the commencement of this period showed that the patient complained of "indigestion" and headache, and the tongue was slightly furred, and anorexia was increasing. On this account he was ordered into the grounds for the whole day and told to take a little exercise, the result being that both his digestion and appetite improved.

Period C.—As the patient's condition and appetite had been improved by being allowed out during the day, and by being allowed to take a little exercise, it was decided to increase his diet in this period, especially as regards the quantity of carbohydrates. The average quantity of

proteids taken daily was 169·31 grammes, an increase of 26·31 grammes over that given in period B, while the quantity of fats was increased by 20·39 grammes, the total quantity taken daily being 203·42 grammes. The daily quantity of carbohydrates was 283·28 grammes, the considerable addition of 71·41 grammes being made to the daily diet in this constituent. The average total number of calories contained in this diet was 3747·43, an increase of 482·28 over the previous period, and the number of calories per kilo. body-weight was 54·85, so that this latter was approximately the same as in the former diet. Owing to an increased quantity of milk being given daily, the average quantity of fluids consumed increased to 2474 c.c.

The quantity of nitrogen contained in the above diet was 26·77 grammes, and as 24·37 grammes were found in the urine, and 1·59 grammes in the fæces, therefore the patient was practically on nitrogen equilibrium, as only 0·81 gramme were retained in the body.

The average daily excretion of urine increased from 1101 c.c. to 1506 c.c., that is to say, nearly proportional to the increased quantity of fluids given, while the specific gravity remains practically the same, being 1021.

TABLE 48.—*The Daily Excretion of Nitrogen and Nitrogenous Substances in the Urine in Case* 3 *on Diet C.*

Date.	Nitrogen.	Urea.	Uric Acid.	Ammonia.
22—23 . .	32·39 ...	58·59 ...	1·03 ...	0·37
23—24 . .	22·28 ...	39·13 ...	1·21 ...	0·52
24—25 . .	22·13 ...	40·28 ...	0·89 ...	0·29
25—26 . .	20·67 ...	37·37 ...	0·76 ...	0·40
Average .	24·37 ...	43·84 ...	0·97 ...	0·39

From the foregoing table it will be seen that there was a marked increase in the average quantity of total nitrogen eliminated in the urine *per diem*, 24·37 grammes being excreted as compared with 17·66 grammes in period B. Of this nitrogen, 83·92 per cent. was eliminated in

the form of urea, a very slight diminution as compared with that of the previous period; 1·36 per cent. was eliminated as uric acid, and 1·39 per cent. as ammonia. From these figures it will be noticed that there was a slight increase in the average daily quantity excreted as nitrogen rest, 13·28 grammes as compared with 12·20 per cent. in period B.

The average daily excretion of urea increased from 30·97 grammes to 43·84 grammes. That of uric acid was practically the same, being 0·97 gramme, while that of ammonia increased markedly, being 0·39 gramme as compared with 0·20 gramme in the previous period, the quantity passed on the second day of analysis, 0·52 gramme, being extremely high.

TABLE 49.—*The Daily Excretion of the Inorganic Substances in the Urine in Case* 3 *on Diet C.*

Date.	Phosphoric Acid.	Chlorides.	Sulphates.			
			Total.	Alkaline.	Aromatic.	Ratio.
22—23	3·97	7·79	4·43	4·20	0·23	18·2 : 1
23—24	2·28	6·16	2·24	2·07	0·17	12·3 : 1
24—25	2·54	5·83	2·36	2·21	0·15	14·7 : 1
25—26	2·45	6·20	2·88	2·74	0·14	19·6 : 1
Average	2·81	6·47	2·98	2·81	0·17	16·5 : 1

On turning to the consideration of the inorganic constituents of the urine, we find that there was a further rise in the average daily elimination of phosphoric acid, the quantity (2·81 grammes) being practically normal, and showing a rise of 0·35 gramme over the previous week. In this week, again, there was a marked increase in the excretion of the chlorides on increasing the diet, the average amount eliminated *per diem* being 6·47 grammes in comparison with 4·65 grammes in period B.

The average excretion of total sulphates in the urine did not show so great an increase as might have been expected from the excretion of total nitrogen in the urine, as only 2·98 grammes were found, this being a slight in-

crease over that of the previous period (2·89 grammes). Of this quantity 2·72 grammes were represented by the alkaline sulphates, so that the average quantity of the aromatic sulphates found (0·17 gramme) remained the same as in period B. Consequently the ratio (16·5 : 1) of the alkaline to the aromatic sulphates showed a further slight increase.

TABLE 50.—*The Daily Excretion of Nitrogen and Fats in the Fæces in Case 3 on Diet C.*

Date.	Quantity.	Water per cent.	Nitrogen.	Fats.
22—23	259	82·88	1·72	7·54
23—24	246	76·65	2·22	9·77
24—25	141	81·93	0·94	4·33
25—26	214	81·43	1·47	6·79
Average	213	80·70	1·59	7·11

It will be seen from the foregoing table that there was a considerable increase in the average daily quantity of nitrogen excreted in the fæces, 1·59 as against 0·96 gramme, and the quantity found exceeded the normal limits, even when the quantity of proteids ingested is taken into consideration. There was also a noteworthy increase in the daily average quantity of fats (7·11 grammes), being more than double that of the last period, and the results obtained in this period appear to be more comparable, as will be seen later, with normal persons on forced feeding than with patients suffering from pulmonary phthisis.

TABLE 51.—*The Daily Diet and Percentage of Nitrogen and Fats absorbed in Case 3 on Diet C.*

Date.	Nitrogen in diet.	Fats in diet.	Nitrogen absorbed per cent.	Fats absorbed per cent.
22—23	26·53	203·76	93·52	96·29
23—24	26·69	186·58	91·68	94·76
24—25	27·27	220·14	96·55	98·03
25—26	26·58	203·19	94·47	96·66
Average	26·77	203·42	94·06	96·44

As was to be expected from the increased quantity of nitrogen found in the fæces, there was a diminution in the percentage of absorption rate, 94·06 per cent. as compared with 95·79 per cent. in period B; and the absorption of this substance was tending to fall decidedly below normal limits. Although the absorption of fats diminished to 96·44 per cent., as compared with 98·28 per cent. in the previous period, still the rate found during this week cannot be considered below the normal limits.

The gain in weight, on comparing the last day of the previous period with that of this one, was 0·57 kilo., the actual weight of the latter day being 66·83 kilos., practically the same increase as is to be found on comparing the average weights during the four days of analysis in the two periods, the weight being 66·5 kilos., as against 65·8 kilos. in period B; the gain was 0·7 kilo.

Clinically the patient was much brighter, the headache having entirely disappeared, and there was practically no further complaint of "indigestion." His appetite was also much improved.

Period D.—In this period it was decided to continue on the same lines as in the last period of Case 2, that is, to keep the quantity of proteids practically the same, to slightly diminish the fats, and to increase considerably the quantity of carbohydrates. On the last two days of the analytical period, however, this patient took fats and carbohydrates badly, so that the following amounts only were obtained:—The quantity of proteids was practically the same as in the last period, being 167·19 grammes, that of the fats 162·87 grammes—a decrease of 40·55 grammes, while the average increase in the quantity of the carbohydrates was only 34·48 grammes, the total daily quantity taken being 317·76 grammes. The average total number of calories contained in this diet was 3482·49, that is, a decrease of 256·01 as compared with period C, while the number of calories per kilo. body-weight was 51·21. There was, however, an increase in the daily

average quantity of fluids taken from 2474 c.c. to 2726 c.c.

The above diet contained an average of 25·95 grammes of nitrogen, and since 22·87 grammes of this substance were found in the urine and 1·09 grammes in the fæces, there was only a retention of 1·18 grammes in the body, so that this patient, during this period, may be considered to have been almost on nitrogen equilibrium.

The average daily excretion of urine rose considerably in this period, being 1943 c.c., the quantity passed on the last day being extremely large (2640 c.c.). This average increase was proportionately greater than the extra quantity of fluids taken, and this was the only instance in which such an occurrence was noted. The average specific gravity, however, diminished more than could be accounted for by the increased quantity of urine passed, as it was only 1014.

TABLE 52.—*The Daily Excretion of Nitrogen and Nitrogenous Substances in the Urine in Case 3 on Diet D.*

Date.	Nitrogen.	Urea.	Uric acid.	Ammonia.
29—30	24·48	45·56	0·97	0·31
30—31	18·65	30·78	0·98	0·47
31— 1	20·35	35·34	0·93	0·37
1— 2	27·98	47·78	1·27	—
Average	22·87	39·87	1·04	0·38

The excretion of total nitrogen in the urine varied considerably, being between 18·65 grammes and 27·91 grammes, and the average of the four days was 22·87 grammes—a slight decrease compared with that found in period C. Of this nitrogen 81·55 per cent. was eliminated in the form of urea—a slight decrease when compared with the 83·92 per cent. absorbed in the previous period, while the amounts excreted in the forms of uric acid and ammonia (1·53 per cent. and 1·54 per cent. respectively) showed a slight increase.

The average daily excretion of urea was 39·87 grammes, that of uric acid increasing from 0·97 gramme to 1·04 grammes, while that of ammonia (the mean of three days' analysis) was practically the same, 0·38 gramme.

TABLE 53.—*The Daily Excretion of the Inorganic Substances in the Urine in Case* 3 *on Diet D.*

Date.	Phosphoric acid.	Chlorides.	Sulphates.			
			Total.	Alkaline.	Aromatic.	Ratio.
29—30	2·48	6·48	3·33	3·17	0·16	19·8 : 1
30—31	2·62	6·07	3·01	2·81	0·19	15·7 : 1
31— 1	2·66	4·44	3·63	3·44	0·19	17 : 1
1— 2	3·96	13·46	4·43	4·17	0·26	16 : 1
Average	2·91	7·61	3·60	3·40	0·20	17 : 1

In contradistinction to the decrease observed in the nitrogen-containing constituents of the urine, there was a slight increase in the amount of phosphoric acid found, a daily average elimination of 2·91 grammes being observed. There was also a further increase in the average quantity of chlorides excreted, 7·61 grammes being eliminated *per diem* as compared with 6·47 grammes in period C.

The daily average excretion of total sulphates in the urine showed an increase from 2·98 grammes to 3·60 grammes, so that proteid metabolism at this period was much more active than in any of the previous ones. The distribution of the sulphates in the urine was as follows :— 3·40 grammes were excreted in the form of alkaline sulphates, and 0·20 gramme in the aromatic group, so that the ratio of the former to the latter again increased slightly, being 17 : 1, as compared with 16 : 5 in period C.

TABLE 54.—*The Daily Excretion of Nitrogen and Fats in the Fæces in Case* 3 *on Diet D.*

Date.	Quantity.	Water per cent.	Nitrogen.	Fats.
29—30	238	75·04	2·43	8·68
30—31	91	84·93	0·56	2·00
31— 1	225	79·21	1·92	6·84
1— 2	301	78·59	2·68	9·42
Average	214	79·44	1·90	6·74

The average daily excretion of nitrogen in the fæces showed a considerable rise, 1·90 grammes being found as against 1·59 grammes in the previous period, and thus there was an increased waste of proteid material. The average daily excretion of fats fell slightly, being 6·74 grammes as compared with 7·11 grammes in period C. But this quantity was still rather above the normal amount, even considering the comparatively speaking large quantity of fats given in the diet.

TABLE 55.—*The Daily Diet and Percentage of Nitrogen and Fats absorbed in Case* 3 *on Diet D.*

Date.	Nitrogen in diet.	Fats in diet.	Nitrogen absorbed per cent.	Fats absorbed per cent.
29—30	26·80	185·80	90·93	95·33
30—31	26·49	197·16	97·89	98·98
31— 1	25·03	139·63	92·33	95·11
1— 2	25·46	128·90	89·47	92·69
Average	25·95	162·87	92·66	95·53

As was only to be expected from the large quantity of nitrogen found in the fæces, and also from the slightly smaller amount of this substance given in the diet, there was a further decrease in the absorption in this period, since only 92·66 per cent. was absorbed, showing that the quantity of proteids given was considerably in excess of the amount that the intestinal tract could deal with effectively. There was also a further diminution in the

absorption of fats—95·53 per cent. as compared with 96·44 per cent. in the previous period, this being despite a considerable diminution in the quantity of fats ingested.

On the last day of this period the patient weighed 67·05 kilos., so that the gain over the corresponding day of period C was very small, being only 0·22 kilo. However, the increase over the last day of period A was moderately satisfactory, amounting to 1·69 kilos. The average weight of the four days during which analyses were carried out was 68·0 kilos., so that the increase over the corresponding period of the previous week was only 0·2 kilo.

The clinical report for this week was that there was no dyspepsia, that the appetite was good, and that the patient felt very well. He was also taking more exercise.

Summary.—The diet in the first period was the normal one on which the patient had been for some time, and on which he had regained a large part of his lost weight; and he had apparently reached the point when he was unable to continue taking this quantity of food satisfactorily, as in period B, during which we attempted to keep him on the same diet, we found a considerable failure of appetite. However, on ordering him into the grounds and giving him a certain amount of exercise, his appetite and capacity for taking food returned, and he bore the increased diet ordered in period C fairly well; but this was only a temporary effort, as shown in period D, as he was unable to continue on roughly the same quantity of food.

The above considerations appear to show that the limit of "cramming" in this patient had been reached, and, judging from the total amounts of his analyses, he was approaching his normal condition, and probably would have been better from a metabolic standpoint if his diet had been reduced considerably.

The following table shows the differences in the quantities of nitrogen retained in the body on altering the amounts of proteid given.

TABLE 56.—*The Increased or Decreased Quantity of Nitrogen retained in the Body on increasing or decreasing the Amount given in the Diet in Case* 3.

Period.	Increase or decrease in the nitrogen in the food, in grammes.	Increase or decrease in the nitrogen excreted, in grammes.[1]	Increased or decreased amount of nitrogen retained, in grammes.
A	—	—	6·30
B	−0·21	+1·83	−2·04
C	+3·89	+7·34	−3·55
D	−0·82	−1·19	−0·37

It will be seen from the above table that in none of the later periods was there an increased amount of nitrogen retained in the body on altering the quantity of this substance given in the food. In fact, during the periods of C and D, the patient was, as has already been noted, practically on nitrogen equilibrium. Although there was an adverse balance of 2·04 grammes in period B, still the diet in this period appears to have been the most suitable, as over four more grammes of nitrogen were retained in the body *per diem;* and it will be seen later that the rates of absorption of both nitrogen and fats were on the whole more satisfactory in this period.

This diet consisted of 143·00 grammes proteids, 183·03 grammes fat, and 211·87 grammes carbohydrates, the value in calories being 3265·15.

[1] That found in both urine and fæces.

TABLE 57.—*Nitrogen Percentage Table, Case* 3. *The proportion of the total Nitrogen in the Urine Excreted as Urea, Uric Acid, and Ammonia in Case* 3.

Period.	Total Nitrogen in Urine.	Nitrogen as Urea.	Nitrogen as Uric acid.	Nitrogen as Ammonia.	Nitrogen as Nitrogen Rest.
A. .	15·68	84·56	2·15	1·11	12·19
B. .	17·66	84·52	2·01	1·24	12·20
C. .	24·37	83·92	1·36	1·39	13·28
D. .	22·87	81·15	1·53	1·54	15·78

The averages of the periods are here given.

The quantity of nitrogen excreted in the most highly oxidised form (urea) is seen in the above table to be in periods A and B; although the diminution in the two later periods is only slight, still it indicates that the powers of the organism were being rather too highly taxed, and that one of the earlier diets was the more suitable. The quantity of nitrogen excreted as nitrogen rest was practically the same in periods A and B, and the gradual increase in periods C and D also shows that the maximum point of benefit had been passed. This is also borne out by the increase in the quantity of ammonia, which, it will be remembered, rose from 0·20 gramme in period B to 0·39 gramme and 0·38 gramme in periods C and D respectively.

The average excretion of total sulphates showed a progressive increase, indicating the activity of proteid metabolism; but this increase was not so marked in period C as one would have expected from the quantity of nitrogen found in the urine, the metabolism in period D being more active, although there was a lessened excretion of nitrogen in the urine in this period. The average quantity of aromatic sulphates found was within the normal limits in all four periods, and consequently there was no increase of intestinal putrefaction during the period under observation.

The decided increase in the average quantity of nitrogen excreted in the fæces in period C as compared

with period B is of interest, as it shows that the intestinal tract was unable to deal advantageously with even the slightly increased quantity given in the food in this period; while the further increase in period D, even though the patient of his own accord, slightly diminished the quantity ingested, and required persuasion to eat as much as he did, shows the length of time that the intestines required to recover their full activity after overstrain.

The excretion of the fats indicates the same point, and the very marked increase in period C is to be noted, as it shows the patient was getting on to the border line between the normal and pathological states, as far as metabolism was concerned.

The absorption of nitrogen reached its highest level in period B, notwithstanding the patient having complained most of dyspeptic symptoms in this week, and this was evidently the best diet. The only effect of increasing the quantity of proteids in the diet was to diminish the absorption, so that the total increase in the quantity absorbed was very slight.

The absorption of fat was also much better in period B, and although the quantity taken in the food was reduced in periods C and D, the rates of absorption diminished.

From a clinical standpoint, during the first two periods under observation he was no better as regards his appetite and digestive symptoms, but on getting out of doors and taking a certain amount of exercise, he improved very greatly in these respects.

The condition of his lesions improved considerably during the month.

CASE 4.—*Pulmonary Tuberculosis, Chronic, Progressive.*

Clinical history.—Age 34, furnace-worker, he had been failing for five years with cough and expectoration, and for the last three years had been unfit for continuous work. During the twelve months previous to admission he had become much worse in every respect. For the last two months of this period he had been attending as an out-patient; he had only benefited very slightly, although he had gained 0·9 kilo. during this time. His condition on admission on July 20th, 1900, was as follows: —Right lung, extensive infiltration throughout the whole lung, with probable excavation, not now active, of medium size in the upper lobe. Left lung: probable infiltration of lower lobe.

At the commencement of the period of observation he was markedly emaciated, of poor general physique, and had much dyspnœa on exertion. His cough was very troublesome, and his sputum (which averaged 6 drachms daily) contained numerous tubercle bacilli.

The amount of fever was slight, never rising above 100° F. (rectal); the appetite was capricious and bad, and the digestion very poor. He was also subject to attacks of vomiting and diarrhœa; there was a certain amount of cyanosis, and well-marked clubbing of the fingers.

During the three weeks since admission he had been for the most part in bed, and had gained 1·46 kilos., his weight being 53·89 kilos. (in dressing-gown and slippers), and he was at this time 21·78 kilos. below his highest known weight, which was 75·60 kilos. His condition otherwise had remained much the same.

TABLE 58.—*The Various Diets and Number of Calories given in Case 4, together with the percentage of Nitrogen and Fats absorbed, etc.*

Period.	A.	B.	C.	D.
Proteids . . .	110·26	115·87	...	...
Fats	126·20	161·18	...	...
Carbohydrates . .	222·74	219·33	...	...
Total calories . .	2538·86	2873·29	...	...
Calories per kilo. .	48·98	54·83	...	...
Fluids . . .	1896	2064	...	...
Nitrogen in urine .	10·25	6·57	...	...
Urea „ .	18·32	11·62	...	...
Nitrogen in fæces .	1·08	1·10	...	...
Fat in fæces . .	3·27	4·56	...	...
Nitrogen absorbed, per cent. . . .	93·95	94·15	...	...
Fat absorbed per cent.	97·43	97·20	...	...
Weight at end of period	54·11	55·01	...	...

Period A.—During the first week under observation he was kept on the diet on which he had been since his admission, and of which he took on an average, 110·26 grammes proteids, 126·20 grammes fats, and 222·74 grammes carbohydrates; so that this diet was very similar to that taken by Case 1 in period A. The total number of calories contained in this diet was 2538·86, and the number per kilo. body-weight 48·98. The average daily quantity of fluids taken was 1896 c.c.

The average daily amount of nitrogen contained in this diet was 17·42 grammes, and 10·25 grammes of this substance were found in the urine, and 8·08 grammes in the fæces, so that 6·09 grammes were retained in the body.

The average daily excretion of urine was 1293 c.c., so that it was rather low in comparison with the quantity of fluid taken. The average specific gravity was 1014.

TABLE 59.—*The Daily Excretion of Nitrogen and Nitrogenous Substances in the Urine in Case 4 on Diet A.*

Date.	Nitrogen.	Urea.	Uric acid.	Ammonia.
8— 9	7·61	15·23	0·24	0·14
9—10	10·25	17·66	0·44	0·19
10—11	9·45	16·13	0·39	0·13
11—12	13·67	24·26	0·66	0·21
Average	10·25	18·32	0·43	0·17

In this case the quantity of total nitrogen excreted in the urine was low, the average being only 10·25 grammes. The daily quantities of nitrogen found varied from 7·61 grammes to 13·67 grammes, so that this patient showed great irregularity as to the manner in which he utilised the proteids given in thé food. The distribution of the nitrogen amongst the various nitrogenous constituents of the urine was as follows:—84·07 per cent. was excreted in the form of urea, 1·37 per cent. in the form of uric acid, 1·36 per cent. in that of ammonia; so that the quantity excreted in the form of nitrogen rest was 13·28 per cent.

The excretion of urea averaged 18·32 grammes per diem, that of uric acid 0·43 gramme per diem, and that of ammonia 0·17 per diem.

TABLE 60.—*The Daily Excretion of the Inorganic Substances in the Urine in Case 4 on Diet A.*

Date.	Phosphoric acid.	Chlorides.	Sulphates.			
			Total.	Alkaline.	Aromatic.	Ratio.
8— 9	1·20	2·92	1·33	1·25	0·08	15·9 : 1
9—10	2·12	6·05	2·11	2·20	0·11	17·3 : 1
10—11	1·06	4·50	—	—	—	—
11—12	2·14	6·02	2·62	2·43	0·19	12·8 : 1
Average	1·63	4·87	2·02	1·89	0·13	14·5 : 1

On turning to the inorganic constituents of the urine, it will be noticed that the excretion of phosphoric acid

was very low on the first and third days of this period, while on the second and fourth it was still below normal, though practically double that of the two days first mentioned. The average daily elimination of this substance only amounted to 1·63 grammes. The excretion of the chlorides—except on the first day, when it was low, being only 2·92 grammes—was about that which is found in the other cases, and the daily average elimination of this substance was 4·87 grammes. The excretion of the total sulphates in the urine was also low in this period, the daily average being only 2·02 grammes (the mean of three analyses), so that this further shows a small amount of proteid metabolism going on in the body. Of this quantity 1·89 grammes was excreted in the form of alkaline sulphates; therefore the amount of aromatic sulphates passed per diem (0·13) was low. The ratio of the alkaline to the aromatic sulphates was 14·5 : 1, thus being within the normal limits.

TABLE 61.—*The Daily Excretion of Nitrogen and Fats in the Fæces in Case 4 on Diet A.*

Date.	Quantity.	Water per cent.	Nitrogen.	Fats.
8—9 ...	160 ...	76·98 ...	1·58 ...	4·79
9—10 ...	54 ...	76·22 ...	0·55 ...	1·67
10—11 ...	118 ...	78·33 ...	1·09 ...	3·33
11—12 ...	117 ...	78·33 ...	1·08 ...	3·30
Average ...	113 ...	77·47 ...	1·08 ...	3·27

The quantity of nitrogen excreted in the fæces varied considerably, from 0·55 gramme on the second day to 1·58 gramme on the first day of analysis, and the average excretion of this substance per diem was 1·08 gramme, that is to say, about the normal. The average daily excretion of the fats was 3·27 grammes, and the eliminations of these substances show a considerable amount of variation, from 4·79 grammes to 1·67 gramme, the average for the four days being roughly about the normal.

TABLE 62.—*The Daily Diet and Percentage of Nitrogen and Fats absorbed in Case 4 on Diet A.*

Date.	Nitrogen in diet.	Fats in diet.	Nitrogen absorbed per cent.	Fats absorbed per cent.
8—9	18·69	128·55	91·83	96·27
9—10	16·69	124·09	96·76	98·65
10—11	17·73	127·08	93·85	97·43
11—12	16·56	125·07	93·37	97·36
Average	17·42	126·20	93·95	97·43

On turning to the consideration of the absorption of the proteids, it will be seen that the average rate (93·95 per cent.) found in the case of nitrogen was decidedly below the normal, while that of the fats, as usually found, was very satisfactory, the average daily excretion being 97·43 per cent.

Throughout the whole of this week the patient's weight remained practically the same, and on the last day the recorded weight was 51·83 kilos. the average for the four days during which he was on analysis being 51·74 kilos.

The clinical report was as follows:—The patient took his food badly, and complained a good deal of "dyspeptic symptoms."

Period B.—Owing to the unsatisfactory condition of the patient during the previous week, and the great difficulty which was experienced in persuading him to take the required quantity of food, it was decided to make only a slight alteration in the diet during this week, and the average quantity of proteids given per diem was only very slightly increased, being 115·87 grammes. The daily quantity of fats taken on the four days during which analyses were carried out was 161·18 grammes, so that there was an increase of 34·98 grammes given per diem. The average daily quantity of carbohydrates remained practically the same, being 219·33 grammes. The total number of calories contained in this diet was 2873·29, there being an increase of 334·43 over period A, while

the number of calories per kilo. body-weight increased from 48·98 to 54·83. During this week the average daily quantity of fluids taken was 2064 c.c.

The average daily quantity of nitrogen contained in the above diet was 18·54 grammes, and since only the very small quantity of 6·57 grammes of this substance was excreted in the urine, and 1·10 gramme in the fæces, 10·87 grammes were retained in the body, as compared with 6·09 grammes in the previous week.

Notwithstanding the increased quantity of fluids given, the average daily excretion of urine diminished from 1293 c.c. to 1000 c.c., although the patient did not complain of night-sweats, or perspirations during the daytime. The average specific gravity also diminished in this period to 1010, as compared with 1014 in period A.

TABLE 63.—*The Daily Excretion of Nitrogen and Nitrogenous Substances in the Urine in Case 4 on Diet B.*

Date.	Nitrogen.	Urea.	Uric acid.	Ammonia.
15—16	5·12	8·51	0·19	0·13
16—17	7·86	14·64	0·26	0·17
17—18	7·90	14·64	0·39	0·13
18—19	5·40	8·69	0·19	0·20
Average	6·57	11·62	0·26	0·16

During this week, the average quantity of total nitrogen excreted in the urine fell markedly, and only reached the low figure of 6·57 grammes, the daily excretion remaining fairly equal throughout the four days. The distribution of this substance was as follows: 81·51 per cent. was eliminated in the form of urea, 1·30 per cent. in that of uric acid, and 2·07 per cent. in that of ammonia, the last-named percentage being a considerable increase over that found in period A, while the percentages of urea and uric acid showed slight diminution. The quantity of nitrogen eliminated in the form of nitrogen rest increased, being 15·13 per cent., as compared with 13·20 per cent. in the previous record.

The average daily excretion of both urea and uric acid diminished considerably, only 11·62 grammes of the former, and 0·26 gramme of the latter being excreted, while that of the ammonia remained practically the same as in period A (0·16 gramme).

TABLE 64.—*The Daily Excretion of the Inorganic Substances in the Urine in Case 4 on Diet B.*

Date.	Phosphoric Acid.	Chlorides.	Sulphates. Total.	Alkaline.	Aromatic.	Ratio.
15—16	0·97	2·19	0·85	0·77	0·08	9·6 : 1
16—17	1·46	3·34	1·37	1·32	0·05	26·4 : 1
17—18	1·32	2·28	1·45	1·33	0·12	11·1 : 1
18—19	0·91	2·39	0·91	0·84	0·07	12 : 1
Average	1·17	2·55	1·15	1·07	0·08	13·4 : 1

It will be seen from the above table that the average daily quantity of phosphoric acid excreted was only 1·17 gramme, and on the first and last days of this period the excretion was very small, being less than 1 gramme. There was also a very marked decrease in the average daily excretion of chlorides, this amounting only to 2·55 grammes, being the lowest average that was obtained in this observation. As will be seen from the very low quantity of total sulphates, excreted in the urine (1·15 grammes) the metabolism of proteid material during this period was at a minimum. 1·07 grammes of this total amount was excreted in the form of alkaline sulphates, and the extraordinarily small quantity of 0·08 gramme of aromatic sulphates was found. The relation of the latter to the former still remained about normal, being 13·4 : 1.

TABLE 65.—*The Daily Excretion of Nitrogen and Fats in the Fæces in Case 4 on Diet B.*

Date.	Quantity.	Water per cent.	Nitrogen.	Fats.
15—16 ...	159 ...	82·12 ...	1·22 ...	5·07
16—17 ...	87 ...	80·21 ...	0·74 ...	3·07
17—18 ...	86 ...	80·21 ...	0·73 ...	3·04
18—19 ...	114 ...	65·29 ...	1·69 ...	7·06
Average ...	114 ...	75·87 ...	1·10 ...	4·56

On turning to the consideration of the fæces, it will be seen that there was practically no change in the average daily excretion of nitrogen in this manner, between the two periods, as 1·10 grammes were found in this week. The excretion of fats, however, rose, especially on the last day of the analytical period, when 7·06 grammes were found, the daily average being 4·56 grammes.

TABLE 66.—*The Daily Diet and Percentage of Nitrogen and Fats absorbed in Case 4 on Diet B.*

Date.	Nitrogen in diet.	Fats in diet.	Nitrogen absorbed per cent.	Fats absorbed per cent.
15—16 ...	19·12 ...	178·24 ...	93·62 ...	97·16
16—17 ...	17·40 ...	144·95 ...	95·72 ...	97·88
17—18 ...	18·38 ...	162·78 ...	96·03 ...	98·13
18—19 ...	19·25 ...	154·74 ...	91·24 ...	95·63
Average ...	18·54 ...	161·18 ...	94·15 ...	97·20

The average rate of absorption of nitrogen improved slightly, from 93·95 per cent. to 94·15 per cent. but this latter quantity still remained below the normal amount, despite the increase in the quantity of fats eliminated. The rate of absorption of this substance remained practically the same, being 97·20 per cent., as against 97·43 per cent. in period A, and there was a considerable increase in the quantity of fats given in the food, so the total amount of this constituent was considerably increased.

On comparing the weights of the last days of periods A and B, it will be seen that there was a satisfactory in-

crease, amounting to 0·9 kilo. The average weight of the four days of analysis was 52·4 kilos., and thus there was a gain of 0·7 kilo. in this latter period as compared with that of the previous week.

Clinically, the condition of the patient was not satisfactory, as the dyspeptic symptoms remained about the same, and his appetite was so poor that he could not eat anything like the quantity of food prescribed.

Summary.—As has just been mentioned, this patient either could not or would not take the prescribed diets, and we have been obliged to omit the last two periods on account of his unsatisfactory behaviour, as, despite the careful attention of the nurses, we could not be certain that he was obeying the regulations as to the collection of the urine and fæces.

During period B there was a satisfactory increase in the quantity of nitrogen retained in the body, as it will be seen from the above table that very little extra of this substance was given in the diet, while practically 3 grammes more were retained.

The marked drop in the excretion of total nitrogen which has been already pointed out is impossible to explain, as the surroundings of the patient remained practically the same throughout the fortnight, and there was no cause at all that could be discovered for its diminution, which appears to be rather similar to that found in the metabolism of people who are taking no food at all.

TABLE 67.—*The Proportion of the Total Nitrogen in the Urine excreted as Urea, Uric Acid and Ammonia in Case* 4.

Nitrogen Percentage Table.

Period.	Total nitrogen in urine.	Nitrogen as urea.	Nitrogen as uric acid.	Nitrogen as ammonia.	Nitrogen as nitrogen heat.
A. ...	10·25	84·07	1·37	1·36	13·20
B. ...	6·57	81·51	1·30	2·07	15·13

The averages of the periods are here given.

The percentage of nitrogen excreted in the most highly oxidised form (urea) was fairly satisfactory in this patient, and there was no marked rise in the proportion eliminated in the form of nitrogen rest, which would be expected if the physical condition was altering very much for the worse.

The excretion of the sulphates in the urine shows that the breaking-up of the proteids was very small, especially in period B; while the very small quantity of aromatic sulphates shows that the amount of intestinal putrefaction was diminished considerably below the normal. The average excretion of the nitrogen and the fats remained within the normal limits throughout both periods, but the absorption of nitrogen was always below the normal, though slightly better in period B. The absorption of the fats was also satisfactory during this week, and it will be clear that this was the better of the two diets tried, as there was also the above-mentioned considerable retention of nitrogen. The fact that there was a diminished breaking down of proteids in the body already mentioned, in this period, does not appear to invalidate this conclusion, as the patient was in such a condition that the principal object of treatment at this time was to give him a reserve of proteid in his body to draw upon.

As far as his clinical condition was concerned, the patient remained in much the same state throughout the two weeks that he was under observation.

CASE 5.—*Chronic Pulmonary Tuberculosis, with Recent very Acute Collapse.*

Clinical history.—Age 36, door porter, admitted July 28th, 1900. This patient commenced treatment as an out-patient at the Brompton Hospital in March, 1899, having at that time slight infiltration of the right apex. By July of the same year the physical signs had cleared up, and he ceased attending, and recommenced work. His weight at that time was 64·83 kilos.

He returned again on July 28th, 1900, and was at once admitted. At this time his condition was as follows:—Right lung: extensive infiltration, with softening and excavation of the upper lobe. Left lung: early infiltration of the upper lobe.

At the commencement of the metabolism experiments, his general condition was very bad, his cough was incessant, and often caused vomiting, the sputum was very abundant, averaging 10 oz. daily, and contained very numerous tubercle bacilli. Night sweats were constant and very profuse. He had high remittent fever, dyspnœa was very marked, and he was very anæmic. The appetite was bad, and he suffered from dyspepsia. His weight was 56·39 kilos. (in dressing-gown, etc.), and he had lost 2·03 kilos. since his admission. No albumen or sugar were found in the urine.

TABLE 68.—*The Various Diets and Number of Calories given in Case 5, together with the Percentage of Nitrogen and Fats absorbed, etc.*

Period.	A.	B.	C.	D.
Proteids . . .	114·93	129·87	220·14	251·47
Fats	121·69	127·05	179·91	208·38
Carbohydrates . .	240·13	225·56	264·83	297·26
Total calories . .	2590·26	2654·23	3661·54	4187·73
Calories per kilo. .	44·59	50·27	67·81	77·28
Fluids. . . .	1952	2183	2726	3234
Nitrogen in urine .	13·45	12·93	15·18	18·14
Urea „ .	20·56	22·13	24·52	28·44
Nitrogen in fæces .	1·10	1·16	2·97	2·41
Fat in fæces . .	6·09	2·13	4·41	4·47
Nitrogen absorbed, per cent. . . .	93·36	94·41	91·67	93·93
Fat absorbed per cent..	95·06	98·33	97·54	97·70
Weight at end of period	55·46	54·90	56·03	56·14

Period A.—During this week he was kept on practically the same diet on which he had been since his admission, and the average quantity of food taken daily consisted of 114·13 grammes proteids, 121·69 grammes

fats, and 240·13 grammes carbohydrates. The average total number of calories contained in this diet was 2590·26, and the number per kilo. body-weight 44·59. The average daily quantity of fluids taken was rather large, 1952 c.c., owing to the fact that, in addition to the milk given, the patient drank a considerable quantity of water.

The quantity of nitrogen contained in this diet averaged 18·39 grammes per diem, and as 13·45 grammes of this substance were found in the urine, and 1·10 gramme in the fæces, therefore 3·84 grammes were retained in the body.

The average daily excretion of urine was low, being 1050 c. c., this small amount being probably due to the combination of the night-sweats and the pyrexia. The average specific gravity was 1022, the urine being thus of the febrile type.

TABLE 69.—*The Daily Excretion of Nitrogen and Nitrogenous Substances in the Urine in Case* 5 *on Diet A.*

Date.	Nitrogen.	Urea.	Uric acid.	Ammonia.
8—9 ...	15·66 ...	27·47 ...	1·01 ...	0·14
9—10 ...	12·93 ...	21·88 ...	0·85 ...	0·19
10—11 ...	12·02 ...	20·57 ...	0·77 ...	0·23
11—12 ...	13·17 ...	22·33 ...	0·93 ...	
Average ...	13·45 ...	23·06 ...	0·89 ...	0·19

The quantity of total nitrogen excreted per diem in the urine averaged 13·45 grammes, and this amount was distributed in the following manner:—80·05 per cent. was eliminated in the form of urea, 2·21 per cent. in that of uric acid, and 1·17 per cent. in that of ammonia. Consequently the amount excreted as nitrogen rest was large, the daily average being 16·60 per cent. The daily excretion of urea averaged 23·06 grammes, and that of ammonia 0·19 gramme.*

* The estimation of ammonia was lost on the fourth day of analysis, so that this figure is the mean of three analyses.

TABLE 70.—*The Daily Excretion of the Inorganic Substances in the Urine in Case* 5 *on Diet A.*

Date.	Phosphoric acid.	Chlorides.	Sulphates. Total.	Alkaline.	Aromatic.	Ratio.
8—9 ...	1·41	5·40	2·44	2·17	0·27	8 : 1
9—10 ...	1·76	5·27	2·36	2·13	0·23	9·3 : 1
10—11 ...	1·36	3·10	1·80	1·61	0·19	8·3 : 1
11—12 ...	1·34	4·47	2·06	1·85	0·21	8·8 : 1
Average ...	1·47	4·56	2·17	1·94	0·23	8·6 : 1

It will be seen from the above table that the average excretion of phosphoric acid was rather low, being 1·47 gramme per diem. The excretion of chlorides in the urine averaged 4·56 grammes, and was about that noticed in the first periods of the other cases, this being a large quantity considering the largo amount of sputum expectorated.

The quantity of total sulphates excreted in the urine averaged 2·17 grammes per diem, so that there was a moderate breaking down of proteids. Of this amount 1·94 gramme was excreted in the form of alkaline sulphates, and 0·23 in that of the aromatic group. The ratio therefore of the alkaline to the aromatic sulphates was 8·6 : 1, this ratio being rather below the normal, there being a slightly excessive amount of intestinal putrefaction present.

TABLE 71.—*The Daily Excretion of Nitrogen and Fats in the Fæces in Case* 5 *on Diet A.*

Date.	Quantity.	Water per cent.	Nitrogen.	Fats.
8—9 ...	185	80·15	1·70	8·38
9—10 ...	196	89·32	0·96	4·77
10—11 ...	159	78·21	1·10	7·97
11—12 ...	59	76·11	0·64	3·22
Average ...	150	80·95	1·10	6·09

On turning to the consideration of the fæces, it will be seen that the average daily excretion of nitrogen in

this manner was 1·10 grammes, that is about the normal. The excretion of the fats, however, was rather high, the daily average being 6·09 grammes, and the excretion of this substance showed a considerable amount of variation, between 8·38 grammes on the first day to 3·22 grammes on the last day of analysis.

TABLE 72.—*The Daily Diet and Percentage of Nitrogen and Fats absorbed in Case* 5 *on Diet A.*

Date.	Nitrogen in diet.	Fats in diet.	Nitrogen absorbed per cent.	Fats absorbed per cent.
8—9	19·72	124·87	91·43	93·29
9—10	19·26	124·74	95·02	96·18
10—11	17·16	118·86	90·68	93·29
11—12	17·40	118·26	96·32	97·29
Average	18·39	121·69	93·36	95·01

It will be seen from the above table that the average rates of absorption of both nitrogen and fats were below the normal in this case, that of the former being 93·36 per cent., and that of the latter 95·01 per cent.

On the last day of this week the patient weighed 53·49 kilos., the average weight for the four days of the analytical period being 53·6 kilos.

As far as his clinical condition was concerned, the patient suffered a good deal from dyspepsia, his condition otherwise remaining about the same.

Period B.—Having now obtained some idea as to the patient's metabolism on the diet on which he had been since admission, it was decided to increase the quantity of food in the following manner:—A slight increase was made in the average daily quantity of proteids, the total given being 129·87 grammes, that is an increase of 15·94 grammes over that given in the previous period; the average daily quantity of fats was very slightly increased, 5·36 grammes being added to the previous amount, so that the total here was 127·05 grammes; while the quantity of the carbohydrates was diminished to 225·56 grammes, a diminution effected principally by the patient

himself, as he found great difficulty in taking food containing much of this constituent. This diet gave 2654·23 total calories, that is practically the same as in period A; but, owing to a decrease in the average weight obtained during the first four days of analysis, the number of calories per kilo. body-weight rose to 50·27. There was a slight increase in the average daily quantity of fluids taken, from 1952 c.c. to 2183 c.c.

20·78 grammes was the amount of nitrogen contained in the proteids in the above diet, and 12·93 grammes of nitrogen were excreted in the urine, and 1·16 grammes in the fæces, so that the amount retained in the body was 6·69 grammes, that is, approximately double that retained in period A.

Notwithstanding the increased quantity of fluids taken, the average daily excretion of urine diminished from 1050 c.c. to 935 c.c., while there was an increase in the average specific gravity from 1022 to 1024.

TABLE 73.—*The Daily Excretion of Nitrogen and Nitrogenous Substances in the Urine in Case 5 on Diet B.*

Date.	Nitrogen.	Urea.	Uric acid.	Ammonia.
15—16	13·78	24·02	0·93	0·24
16—17	12·88	22·84	0·77	0·26
17—18	13·32	24·41	0·79	0·36
18—19	11·73	17·25	0·57	
Average	12·93	22·13	0·76	0·29

The diminution in the average daily quantity of total nitrogen excreted in the urine was very slight, being 12·93 grammes as against 13·45 grammes in the previous week. There was also a slight diminution in the amount of nitrogen eliminated in the form of urea, 79·56 per cent. being found in this period, as compared with 80·02 per cent. in the previous week. The proportion eliminated in the form of uric acid also decreased from 2·21 per cent. to 1·96 per cent.; while the quantity eliminated in the form of ammonia was nearly doubled, an average of 2·04 per

cent. being obtained as compared with 1·17 per cent. in period A. There was practically no difference in the proportion excreted as nitrogen rest, the average in this period being 16·44 per cent. The excretion of urea per diem averaged 22·13 grammes as against 23·04 grammes in the previous week, while the uric acid diminished from 0·89 gramme to 0·76 gramme. There was a considerable increase in the average daily quantity of ammonia excreted, 0·29 gramme being passed per diem as compared with 0·19 gramme in the previous period.*

TABLE 74.—*The Daily Excretion of the Inorganic Substances in the Urine in Case* 5 *on Diet B.*

Date.	Phosphoric acid.	Chlorides.	Sulphates. Total.	Alkaline.	Aromatic.	Ratio.
15—16	1·78	3·65	1·99	1·74	0·25	7 : 1
16—17	1·60	4·14	1·92	1·74	0·18	9·6 : 1
17—18	1·33	4·33	2·11	1·85	0·26	7·1 : 1
18—19	1·49	3·10	1·70	1·48	0·22	6·7 : 1
Average	1·55	3·81	1·93	1·70	0·23	7·4 : 1

On turning to the consideration of the inorganic constituents of the urine, it will be seen that there was a very slight difference only in the average daily excretion of phosphoric acid, 1·55 grammes being eliminated in this period as against 1·47 grammes in period A. In common with the other constituents of the urine analysed for, there was a decrease in the quantity of chlorides excreted in the urine, a daily average of 3·81 grammes being found as compared with 4·56 grammes in period A. The excretion of the total sulphates in the urine also showed a diminution, as the daily average fell from 2·17 grammes to 1·93 grammes. Of this amount, 1·70 grammes was eliminated in the form of alkaline sulphates, the quantity of aromatic sulphates remaining the same, 0·23 gramme, this latter quantity being relatively large, although the absolute amount was not above the normal,

* The analysis on the last day of this period was also lost.

and indicated that the amount of intestinal putrefaction going on was considerable. The ratio of the alkaline to the aromatic sulphates diminished in this period from 8·4 : 1 to 7·4 : 1.

TABLE 75.—*The Daily Excretion of Nitrogen and Fats in the Fæces in Case* 5 *on Diet B.*

Date.	Quantity.	Water per cent.	Nitrogen.	Fats.
15—16 ...	100 ...	76·13 ...	1·21 ...	2·22
16—17 ...	100 ...	76·13 ...	1·21 ...	2·22
17—18 ...	73 ...	69·63 ...	1·12 ...	2·06
18—19 ...	72 ...	69·63 ...	1·10 ...	2·03
Average ...	86 ...	72·38 ...	1·16 ...	2·13

The average daily excretion of nitrogen in the fæces remained practically the same in this period, being 1·16 grammes, and was well within the normal limits, considering the fact that the patient was taking a considerable quantity of proteid food. The excretion of the fats in the fæces showed a marked difference from that of period A, since the daily average was only 2·13 grammes, as compared with 6·09 grammes in period A.

TABLE 76.—*The Daily Diet and Percentage of Nitrogen and Fats absorbed in Case* 5 *on Diet B.*

Date.	Nitrogen in diet.	Fats in diet.	Nitrogen absorbed per cent.	Fats absorbed per cent.
15—16 ...	21·33 ...	130·24 ...	94·33 ...	98·29
16—17 ...	19·51 ...	124·29 ...	93·79 ...	98·21
17—18 ...	20·97 ...	124·50 ...	94·66 ...	98·36
18—19 ...	21·31 ...	129·17 ...	94·84 ...	98·42
Average ...	20·78 ...	127·05 ...	94·41 ...	98·33

It will be seen from the above table that the average absorption of nitrogen increased slightly, 94·41 per cent. being absorbed, as compared with 93·36 per cent. in the previous period; but the rate of absorption of this substance still remained below the normal. On account of the slightly larger quantity of fats ingested, and the

marked decrease in the quantity excreted in the fæces, there was a considerable rise in the rate of absorption of this substance, the daily average being 98·33 per cent., as against 95·01 per cent. in period A, so that the intestinal tract had recovered from its temporary inability to utilise these constituents in the food.

On the last day of this period, the weight of the patient was 52·93 kilos., so that there was a decrease of 0·44 kilo. as compared with that of the corresponding day of the previous week. Owing to the condition of the patient, it was not possible to weigh him on each day of the analytical period, so that we were obliged to take the mean of the weights on the first and last days of this time, and this was 52·4 kilos., so that there was a loss of 1·2 kilos. in comparison with period A. The principal part of this loss was during the middle of the week, his weight on the first day of the period being 53·04 kilos.

During this period the clinical report was that the patient was very weak, and had to be entirely confined to bed during the greater part of this time. He also suffered a good deal from dyspepsia. However, it is satisfactory to be able to say that the night-sweats were somewhat diminished.

Period C.—Although the condition of the patient had not been at all satisfactory during the previous week, it was decided to make a marked increase in the diet, and, in order to avoid an excessive bulk of food, some of the increase in proteids was obtained by the use of somatose, 72 grammes of this substance being given daily.

The average quantity of proteids given was 220·14 grammes, an increase of 90·27 grammes over the previous period; that of the fats 179·91 grammes, an increase of 52·86 grammes; and that of the carbohydrates 264·83 grammes, an increase of 39·27 grammes. There was consequently a considerable increase in the total number of calories given in the above diet—3661·54, as compared with 2654·23 in period B. Despite the increase in the average weight of this period, the number of calories per

kilo. body-weight was 67·81 kilos., that is an increase of 17·54 per kilo. over the previous week. Owing to the quantity of milk being increased in this period, the average daily amount of fluids consumed was 2726 c.c., as against 2183 c.c. in period B.

The average quantity of nitrogen in the above diet was 35·23 grammes, and 15·08 grammes of this substance were eliminated in the urine, and 2·97 grammes in the fæces, so that 17·08 grammes were retained in the body. Though this quantity was much greater than that retained in the latter period, it will be seen later—after having discussed the case as a whole—that there is really no advantage gained by the large amount of proteids given in the diet, as a great part of the increase was immediately excreted.

Although there was an increased quantity of urine excreted per diem, the quantity found (1138 c.c.) was very small in comparison with the large quantity of fluid taken. The average specific gravity remained about the same, being 1023; but this is only the average of three days, as there was no record of it on the second day of analysis.

TABLE 77.—*The Daily Excretion of Nitrogen and Nitrogenous Substances in the Urine in Case* 5 *on Diet C.*

Date.	Nitrogen.	Urea.	Uric acid.	Ammonia.
22—23	17·25	27·60	0·78	0·31
23—24	16·68	27·12	0·90	0·41
24—25	13·49	25·56	0·67	0·19
25—26	13·30	19·80	0·88	
Average	15·18	24·52	0·81	0·31

The average quantity of total nitrogen excreted per diem in the urine was 15·18 grammes, an increase, as compared with the 12·93 grammes excreted in period B.; but very small in comparison with the great increase in the quantity taken in the food. This appears to show

that the organism was not capable of responding to the stimulus that nitrogenous materials normally exert in the healthy being. The distribution of this nitrogen was as follows:—75·40 per cent. was eliminated in the form of urea, a considerable drop from that noted in the last period, when 79·56 per cent. was passed in this form. The proportion eliminated in the form of uric acid was 1·79 per cent., and that in the form of urea 1·60 per cent. The proportion excreted in the form of nitrogen rest was considerably increased, amounting to 22·21 per cent., so that nearly a quarter of the total nitrogen excreted in the urine was in a form that showed that it had not been made use of for proper metabolic purposes. This also showed that the liver was unable to deal adequately with the large quantity of proteid given in the diet. The average daily excretion of urea was 24·52 grammes, that of uric acid 0·81 gramme, and that of ammonia 0·31 gramme.*

TABLE 78.—*The Daily Excretion of the Inorganic Substances in the Urine in Case* 5 *on Diet C.*

Date.	Phosphoric acid.	Chlorides.	Sulphates.			
			Total.	Alkaline.	Aromatic.	Ratio.
22—23	1·29	6·39	2·18	1·75	0·43	4·1 : 1
23—24	0·68	5·28	2·41	2·10	0·31	6·8 : 1
24—25	1·64	4·18	2·16	1·90	0·26	6·1 : 1
25—26	1·32	5·28	2·06	1·75	0·31	5·7 : 1
Average	0·94	5·26	2·21	1·88	0·33	5·7 : 1

There was a marked decrease in the daily average excretion of phosphoric acid, only 0·94 gramme being eliminated, as compared with 1·55 grammes in period B, so that there was only a very slight amount of nucleo-albumen being broken up during this week. The increase in the quantity of chlorides, which has been previously

* The analysis of this last-mentioned substance was again lost on the fourth day.

pointed out as having occurred on increasing the diet, was also noticed in this week; a daily average of 5·26 grammes being eliminated, as compared with 3·84 grammes in period B. The average daily excretion of total sulphates in the urine increased slightly, from 1·93 grammes to 2·21 grammes, the proteid metabolism being thus still very small. Of this amount 1·88 grammes was eliminated in the form of alkaline sulphates, there being an increase in the quantity of aromatic sulphates from 0·23 gramme to 0·33 gramme. It was evident from this that the amount of intestinal putrefaction had still further increased during this week, and this is very clearly seen from the small ratio of the alkaline to the aromatic sulphates found (5·7 : 1).

TABLE 79.—*The Daily Excretion of Nitrogen and Fats in the Fæces in Case* 5 *on Diet C.*

Date.	Quantity.	Water per cent.	Nitrogen.	Fats.
22—23 ...	347 ...	81·01 ...	4·48 ...	6·59
23—24 ...	114 ...	77·04 ...	1·78 ...	2·61
24—25 ...	166 ...	91·53 ...	0·95 ...	1·60
25—26 ...	300 ...	77·17 ...	4·65 ...	6·85
Average ...	282 ...	79·44 ...	2·97 ...	4·41

In the above table it will be seen that there was a very marked increase in the average daily excretion of nitrogen in the fæces, 2·97 grammes being eliminated in this manner, as against 1·16 gramme in period B, so that a large quantity of proteids was being passed through the intestines without being utilised.

The quantity of fats excreted per diem was about normal, being 4·41 grammes, an increase over the small quantity (2·13 grammes) found in period B.

TABLE 80.—*The Daily Diet and Percentage of Nitrogen and Fats absorbed in Case 5 on Diet C.*

Date.	Nitrogen in diet.	Fats in diet.	Nitrogen absorbed per cent.	Fats absorbed per cent.
22—23	35·12	176·05	87·24	96·26
23—24	33·56	174·27	94·69	98·50
24—25	35·28	183·33	97·31	99·13
25—26	36·95	185·99	87·42	96·26
Average	35·23	179·91	91·67	97·54

Notwithstanding the increased quantity of proteid given in the food, the average rate of absorption of nitrogen was very low, being only 91·67 per cent. as compared with 94·41 per cent. in the previous week. Although the quantity of fats in the diet was slightly increased, the rate of absorption of this substance diminished slightly, being 97·54 per cent., and was still within the normal limits.

The patient's weight on the last day of this period was 54·05 kilos., so that there was a gain of 1·12 kilos. over the corresponding day of period B; and he had more than regained the loss of that week, as there was an increase of 0·56 kilo. on comparing this day with the corresponding day of period A. During this week we were again unable to weigh him more than twice during the four days of analysis. The mean of these two occasions was 54·0 kilos., there being a gain of 1·6 kilos. as compared with the weight in period B.

Clinically, the patient was still very weak, and practically confined to bed during this period. His general condition was, however, slightly improved, although his dyspepsia remained as bad as ever.

Period D.—As from the clinical report of the previous week it was evident that the patient's dyspepsia did not increase, it was decided to still further increase the diet, principally by the addition of milk; 56 grammes of sugar and 28 grammes of lactose were also given. The average daily quantity of proteids given was increased

by 31·33 grammes, the total amount therefore being 251·47 grammes. An addition of 28·47 grammes of fats was made to the previous diet, the total quantity in this week being therefore 208·38 grammes. The average quantity of carbohydrates given was 297·26 grammes, there being thus an increase of 32·43 grammes. The total number of calories contained in this diet was 4187·73, that is an increase of 526·19 over that of period C; and the number per kilo. body-weight increased to 77·26. The average daily quantity of fluids taken was further increased to 3234 c.c., principally due to the larger quantity of milk ordered.

The quantity of nitrogen contained in the above diet was 40·14 grammes, and since 18·14 grammes of this substance was excreted in the urine, and 2·41 grammes in the fæces, 19·69 grammes were retained in the body. Although the quantity retained was absolutely increased, it will be seen that there was only a very slight proportional increase, when the increased quantity of proteids ingested is taken into consideration.

There was a considerable increase in the average daily quantity of urine excreted, 1673 c.c. being eliminated, as compared with 1138 c.c. in period C, this increase being nearly proportional to the increase in the quantity of fluids given. The average amount still remained very small in comparison with the total amount of liquid drunk. There was a decline in the average specific gravity from 1023 to 1014.

TABLE 81.—*The Daily Excretion of Nitrogen and Nitrogenous Substances in the Urine in Case 5 on Diet D.*

Date.	Nitrogen.	Urea.	Uric acid.	Ammonia.
29—30 ...	24·75 ...	41·40 ...	1·49 ...	0·63
30—31 ...	11·53 ...	20·15 ...	0·68 ...	0·24
31— 1 ...	21·46 ...	26·72 ...	0·99 ...	0·41
1— 2 ...	14·80 ...	25·07 ...	0·92 ...	0·38
Average ...	18·14 ...	28·44 ...	1·02 ...	0·42

The average excretion of total nitrogen in the urine per diem increased from 15·18 grammes in period C to 18·14 grammes in this week, the quantity being low in comparison with the large quantity of proteids taken in the food. The distribution of this nitrogen was as follows:—79·57 per cent. was eliminated in the form of urea, so that the proportion was slightly better than that found in the previous week; the proportion eliminated in the form of uric acid was 1·09 per cent., and that in the form of ammonia 1·87 per cent. In comparison with the large proportion eliminated in the previous week in the form of nitrogen rest, the 16·66 per cent. found in this period showed an improvement; but the amount excreted in this form was still much above the normal. The average excretion of urea was 28·44 grammes.*

The average daily excretion of uric acid increased from 0·81 gramme to 1·02 grammes, that of ammonia being 0·42 gramme.

TABLE 82.—*The Daily Excretion of the Inorganic Substances in the Urine in Case* 5 *on Diet D.*

Date.	Phosphoric acid.	Chlorides.	Sulphates. Total.	Alkaline.	Aromatic.	Ratio.
29—30	1·37	9·47	3·99	3·36	0·63	5·3 : 1
30—31	0·79	2·73	1·97	1·73	0·24	7·2 : 1
31—1	1·75	8·32	3·33	2·92	0·41	7·1 : 1
1—2	1·64	6·17	2·31	2·05	0·26	7·9 : 1
Average	1·39	6·67	2·90	2·52	0·38	6·6 : 1

On turning to the consideration of the inorganic constituents of the urine, it will be seen from the above Table that there was a slight increase in the average daily quantity of phosphoric acid eliminated, but the amount found (1·39 grammes), though satisfactory as compared with the 0·94 gramme found in period C, was still much below the normal quantity. There was a

* On the second day of analysis, the amount of this substance was not estimated.

further increase in the quantity of chlorides eliminated in the urine, the daily average being 6·67 grammes as compared with 5·26 grammes in the previous period. The excretion of total sulphates in the urine showed a daily average of 2·90 grammes, as against 2·21 grammes in the previous period, so that proteid metabolism was more active during this week. Of this amount 2·52 grammes were eliminated in the form of alkaline sulphates, while there was a further increase in the quantity eliminated in the form of aromatic sulphates, the large amount found (0·38 gramme) indicating that there was a further increased amount of intestinal putrefaction. The ratio of the alkaline to the aromatic sulphates showed a slight increase, being 6·6 : 1, as compared with 5·7 : 1 in period C.

TABLE 83.—*The Daily Excretion of Nitrogen and Fats in the Fæces in Case* 5 *on Diet D.*

Date.	Quantity.	Water per cent.	Nitrogen.	Fats.
29—30 ...	138 ...	76·28 ...	2·16 ...	4·25
30—31 ...	138 ...	76·28 ...	2·16 ...	4·25
31—1 ...	163 ...	75·39 ...	2·64 ...	5·22
1—2 ...	144 ...	71·49 ...	2·71 ...	5·34
Average ...	146 ...	74·86 ...	2·41 ...	4·77

From the above table it will be seen that the excretion of nitrogen in the fæces still remained very high, although the average quantity found (2·41 grammes) was slightly lower than that in period C, when 2·91 grammes were found. The quantity of fats excreted per diem was very slightly increased, being 4·77 grammes, as compared with 4·41 grammes in period C.

TABLE 84.—*The Daily Diet and Percentage of Nitrogen and Fats absorbed in Case 5 on Diet D.*

Date.	Nitrogen in diet.	Fats in diet.	Nitrogen absorbed per cent.	Fats absorbed per cent.
29—30	40·79	220·16	94·71	98·07
30—31	39·34	207·57	94·51	97·95
31— 1	40·22	208·48	93·44	97·49
1— 2	40·22	196·90	93·24	97·29
Average	40·14	208·38	93·93	97·70

Although there was a slight increase in the rate of absorption of nitrogen, the quantity found (93·93 per cent.) was still low, but on taking into consideration the extra quantity of nitrogen given in the food, there was a decided increase in the total amount absorbed. There was practically no difference in the rate of absorption of fats in this period, 97·70 per cent. being absorbed as compared with 97·54 per cent. in the previous week.

On the last day of this period the patient's weight was 54·16 kilos., there being a gain of 0·11 kilo. over the corresponding day of period C. On comparing this day with the corresponding day of period A the total increase was only 0·67 kilo., so that in this respect the patient's progress was not satisfactory. On comparing the average weights of the four days during which analyses were carried out in periods C and D, it will be seen that there was an increase in weight of only 0·2 kilo. respectively, the weights being 54·0 kilos. in period C, and 54·2 kilos. in period D.

The clinical report was that the patient was very ill, and though perhaps slightly stronger, could not have continued on the above diet for any length of time, owing to the severe dyspepsia produced.

Summary.—From a clinical point of view this patient's case was hopeless, as he was much below his proper weight, and, in addition, had very high pyrexia, and profound constitutional disturbance.

Throughout the whole month his weight remained

practically stationary, being 53·49 kilos. on the first day, and 54·05 kilos. on the last day of the period under observation. The fluctuations, however, were very large, ranging between 51·91 kilos. and 54·39 kilos. He frequently lost weight during the first part of the period, and regained it during the latter part, or *vice versâ*. The weight therefore gave no help in determining the most advantageous diet for him. As far as the diets were concerned, this case was practically a repetition of Case 1, as, commencing with a diet containing a normal quantity of proteids, a slight excess of fats, and a small quantity of carbohydrates, he came to take—in period D—rather more than double the quantity of proteids, 70 per cent. more of fats, and 20 per cent. more carbohydrates. The total number of calories increased progressively from 2590·26 to 4187·73. The following table shows the quantity of nitrogen contained in the body on increasing the amount in the food.

TABLE 85.

Period.	Increased amount of nitrogen in diet, in grammes.	Increased or decreased amount of nitrogen excreted,* in grammes.	Increased amount of nitrogen retained in the body, in grammes.
A	—	—	+ 3·71
B	+ 2·39	− 0·59	+ 2·98
C	+ 14·45	+ 4·03	+ 10·42
D	+ 4·91	+ 2·43	+ 2·48

* Total excretion in both urine and fæces.

It will be seen from the foregoing table that, on the diet in period B, the retention of nitrogen was satisfactory, as more than the extra quantity given in the food was retained, the excretion being at its minimum in this period. The quantity retained in period C was large, but there was also a great increase—amounting to more than 25 per cent.—in the amount excreted, and therefore a considerable amount of useless work was being thrown on the organism; and, as has already been pointed out in discussing the sulphates of this period, there was a

very excessive amount of intestinal putrefaction caused. On increasing the diet in period D, almost 50 per cent. of the added nitrogen was excreted immediately, so that here also the organism was unduly tasked in order to obtain slightly greater absorption.

TABLE 86.—*The Proportion of the Total Nitrogen in the Urine excreted as Urea, Uric Acid, and Ammonia, in Case* 5.

Nitrogen Percentage Table.

Period.	Total nitrogen in urine.	Nitrogen as urea.	Nitrogen as uric acid.	Nitrogen as ammonia.	Nitrogen as nitrogen rest.
A.	13·45	80·02	2·21	1·17	16·60
B.	12·93	79·56	1·96	2·04	16·44
C.	15·18	75·40	1·79	1·60	22·21
D.	18·14	79·57	1·90	1·87	16·66

The averages of the periods are here given.

It will be seen from the foregoing table that the quantity of nitrogen excreted in the most highly oxidised form (urea) was low in period A, and that it further diminished in periods B and C, as the quantity of this substance in the diet was increased. In period C it was much below the normal, so that it is evident that the liver was unable to fulfil its functions properly, as was also the case in the two former periods. Notwithstanding the increase in the diet in period B, the percentage excreted in this form rose slightly, being practically the same as in period B. The proportion excreted as nitrogen rest was much above the normal throughout all the periods, and reached its maximum in period C, when roughly 22 per cent. of the total nitrogen excreted in the urine was in this form. It will be noticed that the excretion was at its minimum in period B. It is evident that this large quantity of imperfectly oxidised nitrogen circulating in the blood must produce very prejudicial effects on the body, and may explain the fluctuations in and loss of weight noticed in the various periods.

The average excretion of ammonia increased steadily,

and the large quantity excreted in period D showed that the alkalinity of the blood was diminished.

The average excretion of total sulphates was low throughout all the periods, indicating diminished activity of proteid metabolism; but the principal interest centres in the large quantity of aromatic sulphates, both relatively and absolutely. The great increase in the amount of intestinal putrefaction is very apparent on considering these totals. In this connection it is necessary to lay stress on the fact that the ratio of the alkaline to the aromatic sulphates indicated that the increased amount of intestinal putrefaction was greater than would appear from a consideration of the quantity of the aromatic sulphates alone—especially in the first two periods, as the increase in this latter substance was more relative than absolute, on account of the small quantity of total sulphates excreted.

The quantity of nitrogen in the fæces was about normal in period A, and remained much about the same in period B, and then rose markedly in period C, behaving in a similar manner to that noticed in Case I. However, in period D, the further increase noticed in the last-mentioned case was not apparent, there being a slight diminution, although the quantity still remained high. Though the quantity of fats excreted in period A was high from some unknown cause, still the excretion of this substance did not, in the remaining periods, show any decided variation from the normal, although in period B, the quantity excreted was rather low.

The absorption of nitrogen was very low all through, and was at its best in period B. The absorption in this case differs from that in Case 1 in the fact that the lowest rate was not obtained in period D, when the diet was largest, but in the previous period. The absorption of fats was best in period B, but remained about normal in the two following periods. We are unable to offer any explanation of the relatively low percentage absorbed in period A.

From the various constituents alluded to above, it would appear that the best diet in this case was that given in period B, which consisted of a slight excess of proteids and fats, and a rather small amount of carbohydrates. Probably, a slight increase in this diet—about halfway between this and that given in period C—would have shown better results.

It was impossible clinically to compare this case period by period at the end of the four weeks under observation. He was certainly better in general health than at the commencement, although the dyspepsia was as bad as ever. The night-sweats were less severe, and he appeared to be stronger. However, an examination of the lung showed a further spread of the disease.

CASE 6.—*Chronic Progressive Tuberculosis with Partial Arrest.*

Clinical history.—Age 49, engineer, admitted July 16th, 1900. The disease was of ten months' duration, during the last six of which he had been living an open-air life, as far as was possible, in his own home in Barnsbury. During this time he had improved considerably, and had gained 3·38 kilos. in weight. On admission, his condition was as follows :—*Right lung :* early extensive infiltration of the upper lobe, and also of the apex of the lower lobe. *Left lung :* infiltration and some softening, followed by partial arrest in the upper lobe, and infiltration of the lower lobe.

At the commencement of the period of metabolism experiments his general condition showed satisfactory improvement, and he was practically apyrexial ; his appetite was good, but his digestion somewhat faulty, as he was liable to bad attacks of dyspepsia and obstinate constipation. His weight was 63·46 kilos., and he had gained 3·38 kilos. since admission. He was very considerably below his proper weight, his highest known weight (in his clothes) being 88·2 kilos. He spent the whole day in

the hospital grounds, and took a good deal of walking exercise.

TABLE 87.—*The Various Diets and Number of Calories given in Case 6, together with the Percentage of Nitrogen and Fats absorbed, etc.*

Period	A.	B.	C.	D.
Proteids . . .	109·13	131·38	228·44	161·56
Fats	122·86	190·46	197·72	186·49
Carbohydrates . .	245·00	249·04	283·16	267·97
Total calories . .	2594·53	3332·00	3936·35	3495·43
Calories per kilo. .	41·65	52·23	60·01	52·19
Fluids	1917	2166	2802	2723
Nitrogen in urine .	6·79	6·87	10·29	11·12
Urea	11·53	11·93	18·18	18·83
Nitrogen in fæces .	2·14	1·60	2·01	1·29
Fat in fæces . .	8·42	6·72	3·19	4·75
Nitrogen absorbed per cent. . . .	87·40	94·14	94·46	94·50
Fat absorbed per cent. .	93·12	69·44	98·51	97·83
Weight at end of period	64·91	66·60	68·51	68·96

Period A.—During this period the diet remained the same as that which he had taken since admission, and consisted of 109·13 grammes proteids, 122·86 grammes fats, and 245·00 grammes carbohydrates. The total number of calories contained in this diet was 2594·53, and the number per kilo. body-weight 41·65, the diet, therefore, being an ample one for a normal individual on ordinary exercise. The daily average quantity of fluids taken was 1917 c.c.

The quantity of nitrogen contained in this diet was 17·46 grammes, and 6·79 grammes were excreted in the urine, and 2·14 grammes in the fæces, this latter high amount being due to the necessity of using enemata. Therefore, 10·53 grammes were retained in the body.

The average daily excretion of urine was very low, considering the quantity of fluids taken, and only amounted to 973 c.c., while the average specific gravity was also low—1010.

TABLE 88.—*The Daily Excretion of Nitrogen and Nitrogenous Substances in the Urine in Case 6 on Diet A.*

Date.	Nitrogen.	Urea.	Uric acid.	Ammonia.
8— 9	9·91	13·82	0·35	0·088
9—10	5·30	8·74	0·13	0·050
10—11	6·89	12·71	0·38	0·092
11—12	6·05	10·85	0·22	0·099
Average	6·79	11·53	0·27	0·082

The quantity of total nitrogen excreted in the urine per diem was extremely low, only averaging 6·79 grammes, and this quantity was distributed in the following manner:—81·40 per cent. was eliminated in the form of urea, 1·33 per cent. in that of uric acid, and 1·03 per cent. in that of ammonia; therefore the proportion eliminated in the form of nitrogen rest was large, being 16·25 per cent. The average daily excretion of urea was very low, as was to be expected from the small quantity of nitrogen eliminated, and only amounted to 11·53 grammes. The average excretion of uric acid was also small, considering the age of the patient, and only amounted to 0·27 gramme per diem, while that of the ammonia was especially low, being only 0·08 gramme.

TABLE 89.—*The Daily Excretion of the Inorganic Substances in the Urine in Case 6 on Diet A.*

Date.	Phosphoric acid.	Chlorides.	Sulphates.			Ratio.
			Total.	Alkaline.	Aromatic.	
8— 9	1·04	0·98	1·67	1·53	0·14	10·9 : 1
9—10	0·63	2·47	0·87	0·73	0·11	12 : 1
10—11	1·40	2·19	1·38	1·28	0·10	12·8 : 1
11—12	0·94	3·65	1·09	0·96	0·13	7·4 : 1
Average	1·00	2·32	1·25	1·13	0·13	10·8 : 1

It will be seen from the above table that the quantity of phosphoric acid excreted was extremely low, the daily average being only 1·00 gramme. The excretion of chlorides in the urine was below the normal, only averaging 2·32 grammes per diem. In addition, there

was a small excretion of total sulphates in the urine, the daily average being 1·25 grammes, so that the amount of proteid metabolism going on was very slight. The distribution of the total sulphates was as follows :—1·13 grammes were excreted in the form of alkaline sulphates, while the average quantity of aromatic sulphates eliminated was much below the normal, being only 0·13 gramme. This excretion, though really below the normal, was relatively rather large in comparison with the alkaline sulphates, and the ratio of the latter to the former was consequently low, being 8·6 : 1; but no evidence as to an increased amount of intestinal putrefaction being present can be drawn from the above, on account of the small excretion of this substance.

TABLE 90.—*The Daily Excretion of Nitrogen and Fats in the Fæces in Case 6 on Diet A.*

Date.	Quantity.	Water per cent.	Nitrogen.	Fats.
8—9 ...	334 ...	82·03 ...	2·46 ...	9·63
9—10 ...	666 ...	94·89 ...	1·39 ...	5·46
10—11 ...	450 ...	95·91 ...	0·75 ...	2·97
11—12 ...	540 ...	82·06 ...	3·97 ...	15·64
Average ...	498 ...	88·72 ...	2·14 ...	8·42

Since—owing to the constipation—it was necessary to administer enemata during this period, the average daily excretion of nitrogen in the fæces was increased, and amounted to 2·14 grammes per diem. For the same reason, the excretion of the fats was above the normal, the daily average being 8·42 grammes.

TABLE 91.—*The Daily Diet and Percentage of Nitrogen and Fats absorbed in Case 6 on Diet A.*

Date.	Nitrogen in diet.	Fats in diet.	Nitrogen absorbed per cent.	Fats absorbed per cent.
8— 9 ...	18·01 ...	123·89 ...	86·34 ...	92·23
9—10 ...	18·17 ...	123·96 ...	92·35 ...	95·59
10—11 ...	17·69 ...	123·75 ...	95·76 ...	97·62
11—12 ...	15·96 ...	119·82 ...	75·13 ...	87·03
Average ...	17·46 ...	122·86 ...	87·40 ...	93·12

On account of the large quantity of nitrogen excreted in the fæces, the absorption of this substance was very low, being only 87·40 per cent., while that of the fats was also low, being 93·12 per cent.

On the last day of this period, the patient's weight was 62·57 kilos., and the average of the four days on which he was on analysis was 62·3 kilos.

Clinically, the patient did extremely well, except that he was greatly troubled with constipation.

Period B.—Notwithstanding the fact that it had been necessary to administer enemata during the previous week, it was decided to increase the diet; but the one given in this period, although a very generous one, could scarcely be described under the heading of a "cram diet." The average daily quantity of proteids taken was increased to 131·38 grammes; the average quantity of the fats was 190·46 grammes (an increase of 67·60 grammes); and that of the carbohydrates was practically the same as in the previous period. The total number of calories contained in this diet was 3332·00, a considerable increase over the number in the diet in period A, which was 2594·53. Despite the increase in the weight during this period, the number of calories per kilo. body-weight rose from 41·65 to 52·23. The average daily quantity of fluids taken increased from 1917 c.c. to 2166 c.c.

The quantity of nitrogen contained in this diet was 21·02 grammes, and as only 6·87 grammes were excreted in the urine, and 1·60 grammes in the fæces, it follows that 12·55 grammes were retained in the body, that is, proportionately less than in the previous period.

Despite the increase in the daily quantity of fluids, the average quantity of urine passed per diem diminished from 973 c.c. to 795 c.c., while the average specific gravity increased to 1014.

TABLE 92.—*The Daily Excretion of Nitrogen and Nitrogenous Substances in the Urine in Case 6 on Diet B.*

Date.	Nitrogen.	Urea.	Uric acid.	Ammonia.
15—16	8·18	13·47	0·28	0·10
16—17	6·63	11·80	0·26	0·10
17—18	5·14	9·80	0·22	0·09
18—19	7·53	12·66	0·28	—
Average	6·87	11·93	0·26	0·10

It will be seen from the foregoing table that there was practically no change in the average daily excretion of total nitrogen in the urine, 6·87 grammes being eliminated as compared with 6·79 grammes in period A, and it still remained extremely low. The proportion of this substance excreted in the form of urea remained practically the same, being 81·83 per cent., that eliminated in the form of uric acid being 1·29 per cent., and that in the form of ammonia, 1·23 per cent. There was a very slight diminution in the proportion excreted as nitrogen rest, the daily average being 15·65 per cent. as compared with 16·25 per cent. in the previous week. The average daily excretion of urea was 11·93 grammes, that of uric acid 0·26 gramme, and that of ammonia 0·10 gramme, so that the excretion of these three substances was below the normal.

TABLE 93.—*The Daily Excretion of the Inorganic Substances in the Urine in Case 6 on Diet* B.

Date.	Phosphoric acid.	Chlorides.	Sulphates. Total.	Alkaline.	Aromatic.	Ratio.
15—16	1·31	1·38	1·27	1·18	0·09	13·1 : 1
16—17	0·83	2·30	1·46	1·36	0·10	13·6 : 1
17—18	0·79	3·16	0·85	0·75	0·10	7·5 : 1
18—19	1·14	3·70	—	—	—	—
Average	1·02	2·64	1·20	1·10	0·10	11 : 1

On turning to the consideration of the inorganic constituents of the urine, it will be seen that there was also

practically no change in the average quantity of phosphoric acid excreted, as 1·02 grammes were eliminated per diem, the excretion still remaining at its previous low level. There was a slight increase in the excretion of chlorides in the urine, the daily average being 2·64 grammes as against 2·32 grammes in period A. The average daily excretion of total sulphates in the urine remained practically the same, being 1·20 grammes (the average of three days' analyses). 1·10 grammes of this amount was eliminated in the form of alkaline sulphates, so that there was a further slight diminution in the average quantity of aromatic sulphates eliminated, this aromatic group only amounting to 0·10 gramme; the ratio of the alkaline to the aromatic sulphates was therefore 11 : 1.

TABLE 94.—*The Daily Excretion of Nitrogen and Fats in the Fæces in Case 6 on Diet B.*

Date.	Quantity.	Water per cent.	Nitrogen.	Fats.
15—16	190	77·09	1·57	6·56
16—17	397	84·98	2·14	8·99
17—18	398	84·98	2·15	9·02
18—19	66	76·63	0·55	2·32
Average	265	79·57	1·60	6·72

Although it was necessary to give an enema on one occasion in this period, the average excretion of nitrogen in the fæces diminished to 1·60 grammes per diem, this quantity, however, being still considerably above the normal. There was also a diminution in the average excretion of fats, 6·72 grammes being found, as compared with 8·42 grammes in period A; and although the administration of the enema accounted for a certain proportion of this quantity, still some of this amount was probably due to the increased quantity of fats given in the diet.

TABLE 95.—*The Daily Diet and Percentage of Nitrogen and Fats absorbed in Case 6 on Diet B.*

Date.	Nitrogen in diet.	Fats in diet.	Nitrogen absorbed per cent.	Fats absorbed per cent.
15—16	22·30	196·04	92·97	96·65
16—17	23·03	198·16	90·71	95·46
17—18	19·22	175·99	88·87	94·87
18—19	20·52	191·66	97·27	98·79
Average	21·02	190·46	94·94	96·44

It will be seen from the above table that there was a marked increase in the rate of absorption of nitrogen, 94·94 per cent. being absorbed in this period, as compared with 87·40 per cent. in period A. There was also a considerable improvement in the absorption of fats, 96·44 per cent. being absorbed as compared with 93·12 per cent. in the previous week.

The patient's weight on the last day of this period was 64·26 kilos., there being, consequently, a gain of 1·69 kilos. during the week; while, on comparing the average weight of the two four-day periods of analysis, it will be noticed that there was an increase of 1·5 kilos., the weight in this period being 63·8 kilos.

From the clinical standpoint the patient did extremely well, except that he was troubled with constipation. He took his food moderately well, and was not so troubled with dyspeptic symptoms.

Period C.—During this week it was decided to test the effect of a large increase in proteids, together with a very small increase in fats and a moderate one in carbohydrates. In order to effect the increase in proteids 72 grammes of somatose were given each day, and the quantity of milk was increased. The average daily quantity of proteids was increased by 97·06 grammes, the total quantity being 228·44 grammes. The average quantity of fats was increased from 190·46 grammes to 197·72 grammes, and that of the carbohydrates from 249·04 grammes to 283·16 grammes. The total number of

calories amounted to 3936·35, so that there was an increase of 604·35 over the number given in the previous period. Notwithstanding the considerable increase in weight during this period, the average number of calories per kilo. body-weight rose to 60·01. The average daily quantity of fluids taken was 2802 c.c.—a largely increased quantity over that of period B, when 2166 c.c. were taken on an average.

The quantity of nitrogen contained in the above diet was 36·55 grammes, and since 10·29 grammes were excreted in the urine, and 2·10 grammes in the fæces, it follows that the large quantity of 24·25 grammes was retained in the body. The average excretion of urine per diem was 1130 c.c.—a slight increase over that of period B; but if the large increase in the quantity of fluids consumed is taken into account, the increase in quantity is extremely small. There was practically no change in the average specific gravity, which was 1013 as compared with 1014 in the previous week.

TABLE 96.—*The Daily Excretion of Nitrogen and Nitrogenous Substances in the Urine in Case 6 on Diet C.*

Date.	Nitrogen.	Urea.	Uric acid.	Ammonia.
22—23 ...	11·90 ...	21·38 ...	0·37 ...	0·13
23—24 ...	13·30 ...	21·59 ...	0·42 ...	0·09
24—25 ...	8·56 ...	15·25 ...	0·34 ...	0·08
25—26 ...	7·39 ...	14·50 ...	0·29 ...	0·08
Average ...	10·29 ...	18·18 ...	0·36 ...	0·10

There was an increase in the excretion of total nitrogen in the urine, the daily average in this period being 10·29 grammes as compared with 6·8 grammes in the previous week, this being a very small increase when compared with the large extra quantity of nitrogen taken in the diet. The daily fluctuations in the excretion of this substance were very marked, ranging from 7·39 grammes to 13·30 grammes. The distribution of this nitrogen was as follows:—83·58 per cent. was

eliminated in the form of urea, 1·18 per cent. in the form of uric acid, and 70·78 per cent. in that of ammonia. There was a slight further diminution in the proportion excreted as nitrogen rest, the daily average being 14·46 as compared with 15·65 per cent. in period B. The average excretion of urea was 18·18 grammes per diem, that of uric acid 0·36 gramme per diem, and that of ammonia 0·10 gramme per diem.

TABLE 97.—*The Daily Excretion of the Inorganic Substances in the Urine in Case 6 on Diet C.*

Date.	Phosphoric acid.	Chlorides.	Sulphates. Total.	Alkaline.	Aromatic.	Ratio.
22—23	1·60	6·14	2·16	2·00	0·16	12·5 : 1
23—24	1·05	4·43	1·95	1·73	0·22	7·9 : 1
24—25	0·93	3·35	1·45	1·30	0·15	8·7 : 1
25—26	0·84	2·38	1·12	1·05	0·07	15 : 1
Average...	1·11	4·08	1·67	1·52	0·15	10·1 : 1

It will be seen from the foregoing table that the excretion of phosphoric acid still remained extremely low, although the daily average eliminated (1·11 grammes) was slightly above that of the previous week. The excretion of chlorides in the urine showed the usual rise on increasing the diet, and the daily average found (4·08 grammes) was rather less than that noted in the other cases. The quantity of total sulphates excreted in the urine showed an increase, 1·67 grammes being eliminated, on an average, per diem, and of this quantity 1·52 grammes was passed in the form of alkaline sulphates, so that there was a slight increase in the excretion of aromatic sulphates, 0·15 gramme being eliminated as compared with 0·10 gramme in period B. The ratio of the alkaline to the aromatic sulphates remained practically the same, being 10·1 : 1.

TABLE 98.—*The Daily Excretion of Nitrogen and Fats in the Fæces in Case 6 on Diet C.*

Date.	Quantity.	Water per cent.	Nitrogen.	Fats.
22—23 ...	76 ...	65·81 ...	1·84 ...	1·91
23—24 ...	59 ...	76·58 ...	0·94 ...	1·64
24—25 ...	245 ...	73·19 ...	4·46 ...	7·86
25—26 ...	70 ...	83·87 ...	0·78 ...	1·35
Average ...	113 ...	74·86 ...	2·01 ...	3·19

Although there were no enemata administered in this period, the average excretion of nitrogen in the fæces increased to 2·01 grammes per diem, due apparently to the largely increased nitrogen in-taken. On the other hand, the average excretion of fats diminished by half, being only 3·19 grammes per diem as compared with 6·72 grammes in the previous period.

TABLE 99.—*The Daily Diet and Percentage of Nitrogen and Fats absorbed in Case 6 on Diet C.*

Date.	Nitrogen in diet.	Fats in diet.	Nitrogen absorbed per cent.	Fats absorbed per cent.
22—23 ...	36·60 ...	197·99 ...	94·97 ...	99·03
23—24 ...	36·91 ...	209·63 ...	97·45 ...	99·69
24—25 ...	35·78 ...	197·61 ...	87·53 ...	96·02
25—26 ...	36·91 ...	186·63 ...	97·89 ...	99·28
Average ...	36·55 ...	197·72 ...	94·46 ...	98·51

On account of the largely increased quantity of nitrogen taken in the food the rate of absorption of this substance remained practically the same, being 94·46 per cent., so that, although the percentage absorbed remained practically the same, there was a large increase in the total quantity of nitrogen stored up in the body. On account of the greatly diminished excretion of fats in the fæces the rate absorbed of this substance increased considerably, and 98·51 per cent. was absorbed in this period.

On the last day of this period the patient's weight was 66·17 kilos., there being consequently a gain of 1·8 kilos. over the analytical period of the previous week.

Clinically the patient did well, and was not much troubled with constipation. He complained occasionally that the somatose caused some nausea, but there was no vomiting.

Period D.—During this week it was decided to omit the daily dose of somatose, and to keep the remainder of the diet exactly the same, in order to test the effect of this substance on metabolism. Unfortunately the patient did not take his food quite so well, so that there was a slight general decrease in the average quantity of the various constituents. The quantity of proteids taken per diem was 161·56 grammes, that of the fats 186·49 grammes, and that of the carbohydrates 267·97 grammes.

The total number of calories contained in this diet was 3495·43, being 540·92 less than the number in the diet in period C, and 163·43 more than in period B. The average number of calories per kilo. body-weight was 52·19—practically the same as in period B; but there had been a considerable increase in weight since that time. As on an average a smaller quantity of water per diem was taken, the amount of fluid consumed each day was 2723 c.c. as compared with 2802 c.c. in period C.

The quantity of nitrogen contained in the above diet was 25·85 grammes, and 11·12 grammes of this substance was excreted in the urine, and 1·29 grammes in the fæces; so that 13·44 grammes were retained in the body.

Although the quantity of fluid taken diminished slightly, the average daily excretion of urine increased to 1223 c.c. as compared with 1130 c.c. in the previous week; while there was no change in the specific gravity, which averaged 1013.

TABLE 100.—*The Daily Excretion of Nitrogen and Nitrogenous Substances in the Urine in Case 6 on Diet D.*

Date.	Nitrogen.	Urea.	Uric acid.	Ammonia.
29—30	12·74	21·45	0·68	0·09
30—31	9·12	14·16	0·39	0·11
31— 1	9·84	21·36	0·35	0·13
1— 2	12·78	20·87	0·51	0·22
Average	11·12	18·83	0·48	0·14

It will be noticed that there was a slight further increase in the excretion of total nitrogen in the urine, an average of 11·12 grammes being eliminated per diem as compared with 10·29 grammes in the previous period. The distribution of this nitrogen was as follows:—75·75 per cent. was eliminated in the form of urea, a considerable diminution from the proportion (83·58 per cent.) found in period C; 1·44 per cent. was eliminated in the form of uric acid, and 1·05 per cent. in that of ammonia. The proportion eliminated as nitrogen rest rose considerably, and 21·76 per cent. was excreted in this form, showing that a considerable quantity of the nitrogen in the body was not being properly broken up. The average daily excretion of urea was 18·83 grammes;* that of uric acid 0·48 gramme, and that of ammonia 0·14 gramme.

TABLE 101.—*The Daily Excretion of the Inorganic Substances in the Urine in Case 6 on Diet D.*

Date.	Phosphoric acid.	Chlorides.	Sulphates. Total.	Alkaline.	Aromatic.	Ratio.
29—30	1·61	4·68	2·28	2·12	0·16	13·3 : 1
30—31	1·62	3·20	1·66	1·55	0·11	14·1 : 1
31— 1	1·44	3·96	1·68	1·58	0·10	15·8 : 1
1— 2	1·56	5·68	2·28	2·13	0·15	14·2 : 1
Average	1·61	4·38	1·98	1·85	0·13	14·3 : 1

It will be seen from the above table that the excretion of phosphoric acid remained almost the same, the daily average being only 1·61 grammes, so that throughout the whole experiment the elimination of this substance was very low. There was another slight increase in the elimination of chlorides in the urine. Although the amount of proteids given in the diet was diminished, a daily average of 4·38 grammes was found as against 4·08 grammes in the previous period. The average daily excretion of total sulphates in the urine increased from 1·67 grammes to 1·98 grammes; and of this quantity 1·85 grammes were passed in the form

* The average of three days only being given.

of alkaline sulphates. The average excretion of the aromatic sulphates diminished slightly, and the ratio of the alkaline to the aromatic sulphates increased slightly, being 14·3 : 1.

TABLE 102.—*The Daily Excretion of Nitrogen and Fats in the Fæces in Case 6 on Diet D.*

Date.	Quantity.	Water per cent.	Nitrogen.	Fats.
29—30	77	73·36	0·86	3·22
30—31	201	77·41	1·90	6·86
31— 1	129	77·96	1·19	4·46
1— 2	129	77·96	1·19	4·46
Average	134	76·67	1·29	4·75

On turning to the consideration of the fæces, it will be seen that there was a marked decrease in the excretion of nitrogen in this manner, the daily average being only 1·29 grammes as compared with 2·01 grammes in the previous period. On the other hand, there was an increase from 3·17 grammes to 4·75 grammes in the daily average excretion of fats.

TABLE 103.—*The Daily Diet and Percentage of Nitrogen and Fats absorbed in Case 6 on Diet D.*

Date.	Nitrogen in diet.	Fats in diet.	Nitrogen absorbed per cent.	Fats absorbed per cent.
29—30	25·85	186·49	96·67	98·81
30—31	26·01	186·56	92·69	96·22
31— 1	25·70	186·42	95·37	97·68
1— 2	25·85	186·49	95·39	97·61
Average	25·85	186·49	94·50	97·83

The average rate of absorption of nitrogen (94·50 per cent.) was practically the same as in period C; but as the quantity of proteids in the diet had been considerably reduced, there was a considerable diminution in the total quantity absorbed. Owing to the lessened ingestion and increased excretion of fats the rate of absorption diminished from 98·51 per cent. to 97·83 per cent., the latter rate being, however, a satisfactory one.

On the last day of this period the patient weighed 66·62 kilos., and consequently had gained 0·45 kilo. since the corresponding day of period C, the total gain, since the last day of period A, having been 4·05 kilos. The average weight of the four days during which analyses were carried out was 66·6 kilos.—an increase of 1·00 kilo. over that of period C, and a total gain of 4·3 kilos. since the commencement of the experiment.

From a clinical standpoint the patient did extremely well, although he had not quite so much appetite for his food.

Summary.—During the four weeks that this patient was under observation he showed considerable improvement and put on a satisfactory amount of weight, although at the conclusion he was still much below his proper weight.

Although there was a considerable increase in the quantity of the diets ordered in the different periods, the principal object of this was to study the effect of largely increased quantities of proteids, and it had been intended to compare this case with Case 4; however, as already stated, we were unable to carry out the analysis throughout the whole month in the latter, and consequently this case stands more or less alone. The object of diminishing the proteids in the diet in period D was to see the effect, if any, that was produced in the period following the in-take of such a large quantity. As will be seen from the account of period D, there was apparently no difference caused.

TABLE 104.—*The Increased or Decreased Quantity of Nitrogen retained in the Body on increasing or decreasing the Amount given in the Diet in Case* 6.

Period.	Increase in quantity of nitrogen in food (in grammes).	Increase or decrease of nitrogen excreted * (in grammes).	Increase or decrease in nitrogen retained (in grammes).
A	—	—	+ 10·67
B	+ 3·56	− 0·46	+ 4·06
C	+ 15·53	+ 3·83	+ 11·70
D	− 10·70	+ 0·11	− 10·81

From the above table it will be seen that the quantity

* Total excretion in both urine and fæces.

of nitrogen retained in period B was greater than the extra quantity ingested, this being probably due to the previous stimulation of the intestines by the enemata in period A. The increased retention in period C was very considerable, even though the extra quantity taken per diem was large, and the patient was apparently able to deal satisfactorily with the large amount given. In period D the quantity retained diminished *pari passu* with the decreased in-take, and therefore the digestive tract in this case was not apparently injured by the large quantity of proteids given in period C.

The very low excretion of nitrogen in the urine is noteworthy, but it is impossible to explain why there was such a small proteid metabolism, except on the theory that the patient was replacing degenerated cells by active ones, and that nucleo-albumen was being stored up for the future use of the nuclei.

TABLE 105.—*The Proportion of the Total Nitrogen in the Urine excreted as Urea, Uric Acid, and Ammonia in Case* 6.

Nitrogen Percentage Table.

Period.	Total nitrogen in urine.	Nitrogen as urea.	Nitrogen as uric acid.	Nitrogen as ammonia.	Nitrogen as nitrogen rest.
A ...	6·79 ...	81·40 ...	1·33 ...	1·03 ...	16·25
B ...	6·87 ...	81·83 ...	1·29 ...	1·23 ...	15·65
C ...	10·29 ...	83·58 ...	1·18 ...	0·78 ...	14·46
D ...	11·12 ...	75·75 ...	1·44 ...	1·05 ...	21·76

The averages of the periods are here given.

From the foregoing table it will be seen that the proportion of nitrogen excreted in the most highly oxidised form (urea) remained practically equal during periods A and B, and reached its maximum in period C. As has already been mentioned, there had been apparently no ill effects from the large diet in this period, but the marked diminution in the percentage of nitrogen excreted in this form in period D might be taken as evidence to the contrary, if it were not that three clear days had been allowed to elapse

before the analysis in this week was carried out, during which time he had been taking the diet prescribed for this week; and it is hardly conceivable that there could have been perverted metabolism going on for a whole week without some clinical signs being apparent. We are, therefore, unable to offer any explanation of the low percentage in period D. The proportion excreted as nitrogen rest was decidedly above the normal throughout, but it fell to the minimum in period C. As has been mentioned, we know of no explanation of the very large percentage obtained in the fourth period.

The very small quantities of total sulphates passed in the urine of all the periods show that the breaking up of proteids was very slight, and, taken in conjunction with the low excretion of phosphoric acid, confirm the supposition referred to previously, that the proteid was being stored up as nucleo-albumen. The quantities passed as aromatic sulphates were, throughout, below the normal, there being a relative increase only in period A.

As referred to in discussing period A, the quantity of nitrogen excreted in the fæces was large owing to the administration of enemata, and slightly so in the following week owing to the same reason. In the third period it was above the normal, but not markedly so, while in period D it might almost be considered normal on account of the quantity ingested (25·56 grammes). There was consequently no great waste of proteid in this case. The quantity of fats excreted in periods A and B was large owing to the use of enemata, but that in period C was small considering the large quantity taken in the diet; and a similar remark applies also to period D.

The absorption of nitrogen increased from the very low amount in period A to a more normal one in period B, and then remained practically the same in the two later periods, although it was below the normal all through. The absorption of fats was extremely good in period C when it reached its maximum, but was also within normal in periods B and D.

From all the foregoing statements it appears that the best diet in this case was that given in period C, though probably that used in the following week would have given almost as good results.

Clinically the condition of the patient was excellent all through, except for the troublesome constipation of the first two periods, the gain in weight being very satisfactory.

During the period under observation the condition of his lesions improved.

Effect of Forced Feeding on Normal Individuals.

In order to compare the effect of over-feeding on patients suffering from pulmonary tuberculosis with that obtained in ordinary individuals, we think it advisable to give a short account of the results obtained in another series of experiments. The normal metabolism of some individuals having been ascertained, they were placed on diets containing from 60 to 80 calories per kilo. body-weight. These excessive diets were taken with a good deal of difficulty, and the condition of the individuals quickly altered for the worse, although considerable weight (2—3 kilos.) was put on during the six days that the experiment lasted. The bad effect of the diet was shown by the disturbance to digestion caused, as they all suffered a good deal from anorexia and feelings of distension during this period. Also, for some days after the termination of the experiment they suffered considerably from mucous colitis, and it required various periods of time (from 1—3 weeks) for them to get back into their normal condition. In these individuals the retention of nitrogen in the body was extremely small, except when the over-feeding was carried to its utmost extent, as practically the whole of the excess of nitrogen taken in the diet was immediately excreted.

One of the points of interest observed was that, on increasing the quantity of fluids taken, the quantity of

urine excreted per diem increased almost proportionately, and presented a very high specific gravity. There was a very marked increase in the quantity of total nitrogen in the urine, and the proportion of this substance excreted in the form of urea remained practically normal all through, while the proportion excreted as nitrogen rest tended to increase. Contrary to what was to be expected, there was no very marked change in the excretion of uric acid, the quantity of this substance not rising much above that found on ordinary diet; and the same fact was noticed with regard to the excretion of ammonia.

On turning to the inorganic constituents of the urine a very marked increase was noted in the quantity of phosphoric acid, the excretion of this substance increasing nearly threefold. Although no noticeable increase was made in the quantity of salt taken with the food, there was a very marked increase in the quantity of chlorides excreted in the urine, as, instead of the roughly normal quantity of 4 grammes per diem being eliminated, the excretion rose to between 9 and 10 grammes. As was to be expected from the increased proteid metabolism, there was a marked increase in the quantity of sulphates excreted in the urine, and the amount passed in the form of aromatic sulphates remained about normal, though, if we had been able to carry on the experiment for a few days longer, it is probable that these substances would have increased markedly, as there was evidence of increased intestinal putrefaction occurring, in proof of which may be mentioned the alterations observed in the urine when tested for indican. On the three following days the amount of this substance was markedly increased, Jaffé's test giving marked reaction with one drop of the urine.

No marked difference in the excretion of nitrogen in the fæces was noticed on forced feeding, in contradistinction to what was found in tubercular cases. The excretion of fats on the forced diet showed an enormous increase, and on some days more than 20 grammes were excreted in the fæces. This is the direct opposite to what was found in

the tubercular cases, when no marked increase was noticed, even when the normal quantity of fats in the diet was doubled.

As was to be expected from the fact that the excretion of nitrogen in the fæces was not increased during the period of forced feeding, there was a temporary increase in the quantity of this substance absorbed, as the amount taken in the food was very largely increased. The absorption of the fats tended to diminish on forced feeding, though this decrease was not as marked as would be expected from the enormous quantities found. On account of the very great increase in fats in the diet (in some cases as much as 289·15 grammes were taken in the diet, that is to say, roughly, three times the usual quantity) there was a very rapid increase in weight during the period of forced feeding; but this increase was lost in a very short time, the individuals returning to their normal weight in about a week, although effort was made to keep them as much as possible on their normal diet.

In conclusion, as has already been pointed out above, the forced feeding caused a marked deterioration in health in these cases, and it required a considerable amount of time for them to regain their normal health and energy, one of the things most complained of being that they were utterly incapable of doing any work whatsoever.

The tubercular cases, on the other hand, presented an entirely different sequence of events, for a decided increase in the quantity of food taken was well borne by them. We now give a short summary of the more important results obtained in the course of the experiment.

The number of calories per kilo. body-weight which gave the best results was between 50 and 70, as any increase above the latter number was quickly followed by great anorexia and dyspeptic symptoms, and complete inability to take the diet after a few days, in some cases vomiting being caused. When a very large number of calories was given, that is above 70 per kilo., there was a decided increase in weight during the week, but in no case were

the patients as well at the conclusion of this period as when taking a smaller diet. The only exception to this statement was Case 2, and this patient was a growing boy thirteen years of age, who naturally required a good deal more food in proportion to his weight than any of the other five, who were all adults. In this case, in the diet on which he apparently did best, 103·22 calories were given per kilo. body-weight; but, on continuing him on practically the same diet, a smaller quantity was eaten during the following week, as will be seen on referring to the tables in this case, and it appeared to us to be doubtful whether it would not have been advantageous to reduce the diet to a smaller amount after a short period.

As will be pointed out in discussing the excretion and absorption of nitrogen, the diets in the remaining cases, which gave the most satisfactory results, were those in which, as already mentioned, the number of calories did not exceed 70 per kilo. body-weight. This is especially brought out in Case 1, where the clinical condition of the patient was most satisfactory in the second week, where he retained the most nitrogen in his body at a very small expense to his digestive organs. In considering this question of calories, it is important to point out the fact that, as the condition of the patient—as regards his pulmonary disease—improves, it is very important to diminish the quantity of food given, so as to approximate it more closely to the normal standard. Case 3 is a very good example of this, as reducing the number of calories per kilo. body-weight from 56·65 to 49·85 was followed by a better absorption of both nitrogen and fats, while the weight increased more during this week than during any other period in the duration of the experiment.

In the tubercular cases the quantity of urine excreted was low in comparison with the amount of fluids imbibed, even when there were no noticeable night sweats; and there was no proportionate increase on increasing the quantity of fluids. The only exception to this was in

Case 3, when, in the third and fourth periods, the urine increased almost proportionally to the additional quantity of fluids given; but, as has already been mentioned, this case more nearly approached the normal than any of the others.

In comparison with the quantity of nitrogen given in the food, the excretion of total nitrogen in the urine was very low in the worst cases, and increased markedly when the conditions of the lesions improved. Notwithstanding the fact that the patients were on a diet containing a considerable amount of proteid, the excretion of uric acid was not increased more than would be expected, except in cases complicated by fever. On increasing the diets there was, as a rule, a decided increase in the quantity of ammonia excreted in the urine, pointing to diminished alkalinity of the blood.

The proportion of total nitrogen in the urine excreted in the form of nitrogen rest varied considerably, and was decidedly above the normal in all cases, and showed a decided increase when more than 70 calories per kilo. body-weight were given. In some cases—notably Cases 2 and 6—more than 20 per cent. of the total nitrogen was excreted in this form, so that the oxidation processes in the body were not proceeding actively.

As has already been noted by Russian observers, we found that the quantity of phosphoric acid excreted was very small in this disease, in some cases being less than 1 gramme per diem, while in cases with a considerable degree of arrest, the excretion rose to between 2·5 and 3 grammes. The excretion of chlorides was also below the normal in the cases which had the most advanced physical signs, and it was also possible to form an idea as to the bodily condition of the patient by watching the daily excretion of this substance. On increasing the diet there was generally a decided increase in the quantity of chlorides excreted, but in all cases this increase quickly disappeared.

Taken as a whole, the excretion of total sulphates in the urine was small, showing that there was a greatly diminished

pulmonary tuberculosis that we had the opportunity of observing, consisted roughly of about 120 grammes of proteids, 140 grammes of fats, and 300 grammes of carbohydrates. This diet was for a patient weighing 52 kilos., and contained roughly 59 calories per kilo. body-weight.

As an example of the absolute diets given, we will take the second period of Case 1, when 137·5 grammes proteid, 136·46 grammes fats, and 296·32 grammes carbohydrates were given. On this diet, the rate of absorption of nitrogen was 97·45 per cent., and of fats, 98·15 per cent. During the following week the diet of this patient was increased to the following: 222·50 grammes proteids, 183·93 grammes fats, and 321·37 grammes carbohydrates. On this diet he only absorbed 94·20 per cent. of nitrogen, and 97·90 per cent. of fats, so that a considerable quantity of food was being passed through the intestinal tract unutilised; and, in addition, he suffered considerably from anorexia and dyspepsia.

As an example of a "cram" diet, the average daily quantity of food taken during the fourth period by this patient was: 271·13 grammes proteids, 231·22 grammes fats, and 392·17 grammes carbohydrates; and, on this diet, the rate of absorption of nitrogen was only 89·95 per cent., and of fats, 96·91 per cent., so that the quantity of food unutilised was considerably increased. This last diet caused a little vomiting towards the end of this period, and the patient's expression was that he was utterly unable to continue on it; although, if the weight only had been taken into consideration, it would have been considered a very satisfactory one, there being a gain of 2·1 kilos. during the week. On the diet first given, the gain in weight during the week was 1·1 kilos., which was satisfactory, especially as the condition of the patient improved during the period.

The diet given in the second period of Case 3 was as follows: 143·00 grammes proteid, 183·03 grammes fats, and 211·87 grammes carbohydrates; and his rate of absorption of nitrogen was 95·79 per cent., and of fats

98·28 per cent., his average weight during the period being 65·8 kilos. This was the most suitable diet given to him in any period; and the bad effects of trying to increase the quantity of food taken are well brought out by the results obtained in the fourth period, when 167·18 grammes proteids, 162·87 grammes fats, and 317·76 grammes carbohydrates were given. On this diet he only absorbed 92·66 per cent. of nitrogen and 95·53 per cent. of fats, so that practically no advantage was gained from the increased quantity of food given; and, in addition, the digestive system of the patient was seriously disturbed.

The most advanced case of disease that we had under observation was Case 5, and the most suitable diet we found in his case was that given in the second period, when 129·87 grammes proteid, 127·05 grammes fats, and 225·56 grammes carbohydrates were taken. On this diet, although he was entirely confined to bed and had a considerable degree of fever, he absorbed 94·41 per cent. of nitrogen, and 98·33 per cent. of fats. In the following week his diet was increased to 220·14 grammes proteid, 179·91 grammes fats, and 264·83 grammes carbohydrates, and the rate of absorption of nitrogen diminished to 91·67 per cent., and that of the fats to 97·54 per cent., so that the excessive quantity of food produced a worse result.

The above diets have been given as examples of the various ones tried during the course of the research, and we have included the rates of absorption of nitrogen and fats for the purpose of indicating some of the ways in which we based our conclusions as to the most suitable diets for these patients.

Conclusions.

(1) The tuberculous patients showed very satisfactory results, both clinically and experimentally, when their diets were slightly increased above the original, and, since the original diets were their own selection as regards the amount taken, it is evident that the state of the appetite

gives too low an estimate of their requirements. While comparatively large diets were well borne by those much below their weight, they were not so well tolerated by, nor did they give such satisfactory results in, patients up to weight and with arrested disease.

In all cases, however much they were below their proper weight, very large diets gave unsatisfactory results, as, although weight was gained, it was only at the expense of the general health, as indicated by failure of appetite, more marked digestive disturbances, increased intestinal putrefaction, and (in one case) vomiting.

(2) The mediumly large diets gave the best results, and could have been continued with advantage probably for an indefinite period.

(3) In spite of the various clinical conditions of the six patients, and the fact that the digestive system was obviously impaired in two of them at least, the digestion and absorption of both nitrogen and fats was good. This appears to be so even in patients with high pyrexia. The absorption of fats was excellent, although very large quantities were given; *e. g.* even with an intake of 231·32 grammes, 96·41 per cent. was absorbed. This supports the clinical observation that large quantities of fats are well borne in tubercular dietaries.

(4) It is noticeable that, while on the diets that gave the best results experimentally, the patients complained of the least discomfort, and the onset of severe dyspeptic trouble usually coincided with a deterioration in the experimental results.

(5) In at least one case in which the disease was practically arrested, increase in the time spent out of doors, and in the amount of exercise taken, materially improved both the appetite and digestion.

(6) It appears to be advisable to diminish the amount of food as the disease becomes quiescent and the patient approaches normal weight; but even at this period he will require a more substantial diet than in health.

	Normal.	Tuberculous.
Diet.	Took excessive diet with much difficulty and with lasting bad effects.	Took increased diets much better, and only failed with very excessive diets.
Retention of nitrogen.	Very small except on extreme forced feeding.	Considerable in all increased diets, and well marked in some.
Quantity of urine.	Increase more or less proportional to increased intake of fluids.	Very little connection between increase in quantity and increased fluid intake.
Specific gravity.	Very high.	For the most part low.
Nitrogen in urine.	Marked increase on forced feeding.	Below normal, most markedly so in patients much below normal weight, and approaching normal quantity in cases nearly up to their weight.
Urea.	Very large quantities passed on forced feeding. Proportion of nitrogen thus excreted remained normal all through.	Excretion lower than in normal cases on similar diets. Patients with active disease excreted smaller proportion of nitrogen as urea than those with tendency to arrest. This proportion falls further on excessive diets.
Uric acid.	Follows ordinary course.	Smallest excretion met with in those most below weight.
Ammonia.	Did not increase out of proportion on forced feeding.	No disproportionate increase noted. In excessive feeding, large quantities found.
Nitrogen.	Tendency to increase on forced feeding.	Increased on larger diets. Very large in cases with impaired digestion and active disease.
Phosphoric acid.	Marked increase on forced feeding.	Quantity diminished throughout. Only slight increase on larger diet.
Chlorides.	Marked increase on forced feeding.	Usually low on ordinary diets. Increased on increasing the diet, but this not usually maintained.
Sulphates.	Increased by forced feeding. Aromatic—normal. Ratio—normal.	Lowest in worst cases, increasing on larger diets. Aromatic—marked increase on forced feeding. Ratio—diminished on forced feeding.
Nitrogen in fæces.	No marked increase as a rule on forced feeding.	Diminished or normal on ordinary diet. Very marked increase on forced feeding.
Fats in fæces.	Usually an enormous increase on the forced diet.	Diminished or normal on ordinary diets. Increase not marked on excessive feeding.

	Normal.	Tuberculous.
Absorption of nitrogen.	Temporary increase on forced feeding.	Slightly below normal on ordinary diets. Increased on larger diets. Diminished on forced feeding.
Absorption of fats.	Tendency to diminish on forced feeding.	Extremely good all through.
Weight.	Rapid increase on forced feeding, but soon lost.	Satisfactory gain on ordinary diet. Further increase on forced feeding, but at expense of general condition, and could not be maintained.
General.	Forced feeding caused marked deterioration in health.	Stood large diets extremely well, and forced feeding did not cause such marked symptoms, but too many to continue it for long.

Literature.

1. Griezdiev.—Vrach 11, p. 123.

2. Kurlov.—'Inaug. Discuss.,' St. Petersburg, p. 48.

3. Swavastyanov.—'Inaug. Discuss.,' St. Petersburg, p. 48.

4. Blumenfeld (Spirig).—'Beiträge zur Lehre vom Stoffwechsel des Gesundes v. Kranken Menschen,' pt. 3, p. 116.

5. Levin.—Vrach 8, p. 878.

6. Hadley and Goodbody.—'Brit. Med. Journ.,' 1896.

TABLES FOR METABOLISM IN PHTHISIS

CASE

Date.	Diet.				Calories per kilo.	Urine.					
	Nitrogen	Fats	Carbohydrates	Fluids		Quantity	Sp. gr.	Total nitrogen	Urea	Uric acid	Ammonia
Period A.											
8— 9	18·59	123·55	295·07	1952	55·59	2025	1013	16·26	34·02	0·81	0·30
9—10	18·90	123·66	310·47	2176	56·89	1585	1012	13·09	21·19	0·55	0·16
10—11	18·43	123·48	287·37	2148	55·20	1600	1018	19·34	34·97	1·00	0·43
11—12	18·40	122·44	293·91	1840	55·43	1400	1019	17·85	32·62	1·00	0·29
Average.....	18·58	123·28	296·71	2029	55·78	1653	1016	16·64	30·70	0·84	0·30
Period B.											
15—16	21·84	136·89	288·62	2232	58·81	1360	1016	15·23	27·66	0·66	0·23
16—17	21·69	136·82	280·92	1840	57·31	1740	1016	17·75	35·82	0·71	0·34
17—18	22·31	137·10	311·72	2232	59·63	1200	1014	12·45	—	0·65	0·19
18—19	22·16	137·03	304·02	2504	58·96	1670	1012	12·69	23·05	0·55	0·30
Average.....	22·00	136·96	296·32	2204	58·68	1493	1015	14·53	28·84	0·64	0·27
Period C.											
22—23	37·21	186·80	322·87	2922	74·61	1775	1014	18·98	30·59	0·60	0·16
23—24	37·21	186·80	322·87	2782	73·53	2240	1013	23·58	42·11	0·84	0·23
24—25	37·37	186·87	324·57	2614	74·98	1560	1016	18·26	33·69	0·51	0·14
25—26	37·01	175·23	315·17	2922	71·17	2255	1012	22·34	35·85	0·88	0·30
Average.....	37·20	183·93	321·37	2810	73·57	1957	1014	20·82	35·56	0·71	0·21
Period D.											
29—30	43·65	232·86	404·14	3444	88·23	2480	1011	23·33	36·95	0·87	0·35
30—31	43·21	238·49	382·58	3444	87·23	2270	1012	24·34	43·35	0·83	0·31
31— 1	43·65	232·86	406·38	3444	87·88	2160	1012	22·46	38·44	0·73	0·20
1— 2	43·02	221·08	375·58	3444	83·45	2240	1012	25·38	43·72	0·84	0·68
Average.....	43·38	231·32	392·17	3444	86·70	2288	1012	23·88	40·62	0·82	0·39

1.

Urine.						Fæces.				Absorbed per cent.		Weight, kilos.
P_2O_5	Chlorides	Sulphates: Total	Sulphates: Alkaline	Sulphates: Aromatic	Sulphates: Ratio, A : B	Quantity	Water per cent.	Nitrogen	Fats	Nitrogen	Fats	
2·63	4·62	3·20	2·92	0·28	11·1 : 1	520	80·91	3·27	16·11	82·41	86·99	51·0
1·58	4·63	2·66	2·50	0·16	14·4 : 1	102	93·09	0·23	1·14	98·78	99·08	51·1
3·33	7·84	3·58	3·38	0·20	16·9 : 1	410	89·01	1·49	7·26	91·92	94·12	50·7
2·27	6·02	3·21	3·00	0·21	14·3 : 1	410	89·01	1·49	7·26	91·90	94·07	50·8
2·45	5·78	3·16	2·95	0·21	14·0 : 1	361	87·26	1·62	7·94	91·25	93·82	50·9
2·45	4·90	2·69	2·53	0·16	15·8 : 1	103	78·87	0·72	3·27	96·70	97·61	51·3
2·26	3·05	1·99	1·75	0·24	7·3 : 1	103	78·87	0·72	3·27	96·68	97·61	52·0
2·12	6·13	2·82	2·62	0·20	13·1 : 1	72	92·88	0 17	0·75	99·24	99·45	52·4
1·90	5·94	2·89	2·69	0·20	13·5 : 1	48	59·96	0·63	2·83	97·16	97·93	52 4
2·18	5·01	2·60	2·40	0 20	12·0 : 1	82	77·65	0·56	2·53	97·45	98·15	52·0
2·34	6·80	4·75	4·52	0·23	19·9 : 1	186	67·57	3·43	5·07	90·78	97·29	53·8
3·11	13·44	3·96	3·45	0·51	6·8 : 1	164	81·23	1·75	2·59	95·83	98·61	54·6
2·95	8·11	2·90	2·68	0·22	12·2 : 1	137	69·26	2·34	4·94	93·74	97·36	53·7
3·26	7·41	2·89	2·64	0·25	10·5 : 1	58	60·05	1·32	2·93	96·44	98·33	54·4
2·92	8·94	3·62	3·32	0·30	12·4 : 1	136	69·50	2·11	3·88	94·20	97·90	54·1
2·08	9·27	3·90	3·39	0·51	6·6 : 1	200	64·25	3·79	6·67	91·32	97·14	56·0
2·03	7·87	4·52	4·02	0·50	8·0 : 1	235	66·97	4·11	7·24	90·49	96·96	56·1
3·67	4·75	4·08	3·63	0·45	8·1 : 1	303	67·35	5·24	9·89	87·99	95·75	56·3
3·64	11·71	4·59	4·09	0·50	8·1 : 1	252	67·70	4·31	7·59	89·98	96·57	56·3
2·86	8·15	4·27	3·78	0·49	7·7 : 1	248	66·02	4·36	7·85	89·95	96·41	56·2

CASE

Date.	Diet.				Calories per kilo.	Urine.					
	Nitrogen	Fats	Carbohydrates	Fluids		Quantity	Sp. gr.	Total nitrogen	Urea	Uric acid	Ammonia
Period A.											
8— 9	24·14	215·59	258·17	1868	109·26	1785	—	15·48	28·91	0·37	0·33
9—10	23·10	202·15	223·68	1868	101·16	1960	1015	8·64	14·69	0·20	0·30
10—11	23·16	215·84	207·22	1840	102·39	1018	1017	12·43	23·44	0·39	0·22
11—12	22·24	216·33	199·94	1840	100·05	1650	1013	16·28	29·56	0·60	0·28
Average.....	23·66	212·48	222·25	1854	103·22	1353	1015	13·21	24·15	0·39	0·28
Period B.											
15—16	24·76	203·18	228·92	1952	100·65	1550	1012	16·12	28·18	0·39	—
16—17	23·57	205·18	219·57	1880	99·20	1100	1016	12·65	24·19	0·36	0·24
17—18	22·67	187·70	240·53	2008	95·73	950	1020	13·62	26·32	0·56	0·29
18—19	21·92	173·79	184·12	2232	83·39	1300	1013	16·23	29·25	0·56	0·20
Average.....	23·23	192·46	217·04	2043	94·74	1225	1015	14·66	26·99	0·47	0·24
Period C.											
22—23	26·06	186·09	269·51	2586	100·38	1940	1012	17·61	26·38	0·35	0·37
23—24	25·70	169·27	254·17	2586	93·86	1840	1011	15·66	25·39	0·47	0·20
24—25	25·89	193·83	290·78	2586	104·52	1160	1014	14·26	26·68	0·42	0·22
25—26	24·97	167·13	291·22	2586	96·52	1800	1012	18·35	30·96	0·64	0·54
Average.....	25·66	179·83	271·45	2586	98·82	1685	1012	16·47	27·35	0·47	0·33
Period D.											
29—30	25·79	184·66	334·67	2670	106·52	1430	1012	14·13	22·73	0·49	0·42
30—31	25·48	184·52	328·23	2726	105·23	1080	1012	11·10	16·41	0·46	0·27
31— 1	24·14	156·01	297·43	2726	92·39	1160	1012	13·92	19·49	0·50	0·53
1— 2	24·43	139·26	297·43	2670	88·97	2070	1012	18·63	31·05	0·64	0·62
Average.....	25·09	166·11	314·44	2698	98·28	1435	1012	14·22	22·42	0·52	0·46

2.

Urine.						Fæces.				Absorbed per cent.		
P_2O_5	Chlorides	Sulphates: Total	Sulphates: Alkaline	Sulphates: Aromatic	Sulphates: Ratio, A : B	Quantity	Water per cent.	Nitrogen	Fats	Nitrogen	Fats	Weight, kilos.
2·48	9·78	3·02	2·89	0·13	23·0 : 1	150	78·03	1·31	4·36	94·57	97·98	33·7
1·63	2 78	1·82	1·74	0·08	21·7 : 1	116	82·46	0·81	1·89	96·49	99·07	33·5
2·27	3·56	2·37	2·27	0·10	22·7 : 1	81	76·77	0·75	3·36	96·76	98·44	33·7
2·48	6·27	3·05	2·92	0·13	22·3 : 1	122	80·30	0·96	3·17	95·68	98·58	34·0
2·22	5·59	2·57	2·46	0·11	22·4 : 1	117	79·39	0·96	3·20	95·88	98·52	33·7
2·71	5·29	2·81	2·68	0·13	22·2 : 1	109	77·20	1·04	2·68	95·79	98·68	34·2
2·20	4·95	2·67	2·60	0·07	37·1 : 1	128	80·00	1·07	2·86	95·42	96·61	34·4
2·36	3·29	2·51	2·39	0·12	19·9 : 1	83	78·18	0·76	2·04	96·65	99·45	34·6
2·70	3·39	2·38	2·25	0·13	17·3 : 1	89	81·77	0·68	1·81	96·89	98·96	34·8
2 49	4·23	2·59	2·48	0·11	22·5 : 1	102	79·29	0·89	2·45	96·29	98·93	34·5
2·83	7·44	3·02	2·88	0·14	20·3 : 1	130	76·85	1·36	2·46	94·78	98·68	34·9
2·56	5·37	2·82	2·67	0·15	17·8 : 1	128	83·81	0·93	1·69	96·38	99·00	34·9
2·53	5·29	2·83	2·69	0·14	19·2 : 1	123	81·85	1·01	1·92	96 09	98·96	35·0
2·57	6·24	3·42	3·25	0·17	18·6 : 1	137	88·71	0·70	1·26	97·19	99·25	35·1
2·62	6·09	3·02	2·87	0·15	19·1 : 1	130	82·81	1·00	1·83	96·11	98·97	35·0
2·18	3·39	2·42	2·31	0·11	21·0 : 1	144	79·97	1·32	3·21	94·88	98·26	35·3
1·73	3·64	2·04	1·95	0·09	21·7 : 1	140	82·74	1·11	2·80	95·64	98·48	35·3
1·98	2·78	2·44	2·35	0·09	26·1 : 1	98	79·23	0·94	2·26	96·19	98·55	35·6
3·20	7·66	3·13	2·98	0·15	19·1 : 1	114	82·68	0·91	2·20	96·32	98·42	35·3
2·27	4·37	2·51	2·40	0·11	21·8 : 1	124	81·16	1·07	2·62	95·76	98·43	35·4

CASE

Date.	Diet.				Calories per kilo.	Urine.					
	Nitrogen	Fats	Carbohydrates	Fluid		Quantity	Sp. gr.	Total nitrogen	Urea	Uric acid	Ammonia
Period A.											
8— 9	24·72	221·92	255·03	1896	57·20	1500	1015	18·15	32·40	0·75	0·32
9—10	20·66	206·49	238·98	1840	52·60	1000	1025	15·82	28·60	0·88	0·22
10—11	24·24	221·71	219·93	1840	55·07	720	1023	12·24	22·88	1·28	0·13
11—12	22·74	197·14	227·63	1840	51·21	1000	1024	16·52	29·49	0·90	0·19
Average.....	23·09	211·82	235·39	1854	54·02	1055	1021	15·68	28·34	0·95	0·22
Period B.											
15—16	20·92	168·55	189·75	1840	44·60	1400	1018	19·04	33·10	0·84	0·28
16—17	23·59	190·23	244·68	1840	51·24	930	1026	16·00	30·78	0·86	0·14
17—18	22·40	183·29	210·07	2008	47·43	400	1022	7·64	15·08	0·85	0·24
18—19	24·59	190·01	206·98	2176	48·87	1675	1022	27·97	44·90	1·22	0·14
Average.....	22·88	183·03	212·87	1966	48·04	1101	1022	17·66	30·97	0·94	0·20
Period C.											
22—23	26·53	203·76	280·42	2390	56·25	1770	1022	32·39	58·59	1·03	0·37
23—24	26·69	186·58	287·12	2502	54·24	1340	1022	22·28	39·13	1·21	0·52
24—25	27·27	220·14	295·82	2502	59·44	1325	1022	22·13	40·28	0·89	0·29
25—26	26·58	203·19	269·72	2502	55·04	1590	1016	20·67	37·37	0·76	0·40
Average.....	26·77	203·42	283·28	2474	56·24	1506	1021	24·37	43·84	0·97	0·39
Period D.											
29—30	26·80	185·80	359·91	2726	57·04	1800	1014	24·48	45·56	0·97	0·31
30—31	26·49	197·16	344·51	2726	57·70	1480	1017	18·65	30·78	0·98	0·47
31— 1	25·03	139·63	264·91	2726	44·58	1850	1010	20·35	35·34	0 93	0·37
1— 2	25·46	128·90	301·71	2726	45·20	2640	1013	27·98	47·78	1·27	—
Average.....	25·95	162·87	317·76	2726	51·13	1943	1014	22·87	39·87	1·04	0·38

3.

Urine.						Fæces.				Absorbed per cent.		Weight, kilos.
P_2O_5	Chlorides	Sulphates: Total	Sulphates: Alkaline	Sulphates: Aromatic	Sulphates: Ratio, A : B	Quantity	Water per cent.	Nitrogen	Fats	Nitrogen	Fats	
2·38	6·01	3·36	3·19	0·17	18·7 : 1	120	76·08	1·05	5·60	95·75	97·48	65·4
2·38	5·75	2·94	2·77	0·17	16·3 : 1	219	83·74	1·68	7·95	91·87	96·15	65·2
1·73	3·96	2·39	2·15	0·24	8·9 : 1	110	79·20	0·85	4·43	96·49	98·02	65·1
2·16	6·84	2·28	2·62	0·16	16·3 : 1	110	79·20	0·85	4·43	96·26	97·75	65·4
2·16	5·64	2·87	2·68	0·18	14·1 : 1	140	79·67	1·11	5·60	95·09	97·35	65·3
3·08	2·35	2·99	2·79	0·20	13·1 : 1	130	80·01	1·04	3·42	95·03	97·97	64·6
2·07	6·32	2·38	2·21	0·17	12·1 : 1	149	79·22	1·23	4·07	94·78	97·86	65·9
0·88	2·56	1·25	1·18	0·07	17·1 : 1	102	81·16	0·77	2·54	96·51	98·67	66·2
4·19	7·37	4·94	4·70	0·24	19·6 : 1	103	81·16	0·78	2·62	96·83	98·62	66·4
2·56	4·65	2·89	2·72	0·17	16·1 : 1	121	80·13	0·96	3·16	95·79	98·28	65·8
3·97	7·79	4·43	4·20	0·23	18·2 : 1	259	82·88	1·72	7·54	93·52	96·29	66·2
2·28	6·16	2·24	2·07	0·17	12·3 : 1	246	76·65	2·22	9·77	91·68	94·76	66·3
2·54	5·83	2·36	2·21	0·15	14·7 : 1	141	81·93	0·94	4·33	96·55	98·03	66·6
2·45	6·20	2·88	2·74	0·14	19·6 : 1	214	81·34	1·47	6·79	94·47	96·66	66·8
2·81	6·47	2·98	2·81	0·17	16·5 : 1	213	80·70	1·59	7·11	94·06	96·44	66·5
2·48	6·48	3·33	3·17	0·16	19·8 : 1	238	75·04	2·43	8·68	90·93	95·33	68·2
2·62	6·07	3·01	2·82	0·19	15·7 : 1	91	84·93	0·56	2·00	97·89	98·98	68·0
2·66	4·44	3·63	3·44	0·19	17·0 : 1	225	79·21	1·92	6·84	92·33	95·11	67·9
3·96	13·45	4·43	4·17	0·26	16·0 : 1	301	78·59	2·68	9·42	89·47	92·69	68·0
2·91	7·61	3·60	3·40	0·20	17·0 : 1	214	79·44	1·90	6·74	92·66	95·53	68·0

CASE

Date.	Diet.					Urine.					
	Nitrogen	Fats	Carbohydrates	Fluids	Calories per kilo.	Quantity	Sp. gr.	Total nitrogen	Uren	Uric acid	Ammonia
Period A.											
8— 9	18·69	128·55	245·26	1924	51·94	1070	1014	7·61	15·23	0·24	0·14
9—10	16·69	124·09	227·16	1924	48·70	1275	1013	10·25	17·66	0·44	0·19
10—11	17·73	127·08	204·06	1924	47·89	1250	1012	9·45	16·13	0·39	0·13
11—12	16·56	125·07	214·46	1812	47·62	1575	1017	13·67	24·26	0·66	0·21
Average.....	17·42	126·20	222·74	1896	49·04	1293	1014	10·25	18·32	0·43	0·17
Period B.											
15—16	19·12	178·24	236·31	1952	59·70	1000	1006	5·12	8·51	0·19	0·13
16—17	17·40	144·95	198·10	1952	50·12	900	1012	7·86	14·64	0·26	0·17
17—18	18·38	162·78	210·50	2120	54·22	1200	1011	7·90	14·64	0·39	0·13
18—19	19·25	154·74	232·39	2232	54·75	900	1011	5·40	8·69	0·19	0·20
Average.....	18·54	161·18	219·33	2064	54·70	1000	1010	6·57	11·62	0·26	0·16

4.

Urine.						Fæces.				Absorbed per cent.		
P_2O_5	Chlorides	Sulphates: Total	Sulphates: Alkaline	Sulphates: Aromatic	Sulphates: Ratio, A : B	Quantity	Water per cent	Nitrogen	Fats	Nitrogen	Fats	Weight, kilos.
1·20	2·92	1·33	1·25	0·08	15·9 : 1	160	76·98	1·58	4·79	91·83	96·27	51·6
2·12	6·05	2·11	2·20	0·11	17·3 : 1	54	76·22	0·55	1·67	96·76	98·65	51·6
1·06	4·50	—	—	—	—	118	78·33	1·09	3·33	93·85	97·43	51·6
2·14	6·02	2·62	2·43	0·19	12·8 : 1	117	78·33	1·08	3·30	93·37	97·36	51·8
1·63	4·87	2·02	1·89	0·13	14·5 : 1	113	77·47	1·08	3·27	93·95	97·43	51·7
0·97	2·19	0·85	0·77	0·08	9·6 : 1	159	82·12	1·22	5·07	93·62	97·16	52·2
1·46	3·34	1·37	1·32	0·05	26·4 : 1	87	80·21	0·74	3·07	95·72	97·88	52·0
1·32	2·28	1·45	1·33	0·12	11·1 : 1	86	80·21	0·73	3·04	96·03	98·13	52·6
0·91	2·39	0·91	0·84	0·07	12·0 : 1	114	65·29	1·69	7·06	91·24	95·63	52·7
1·17	2·55	1·15	1·07	0·08	13·4 : 1	114	75·87	1·10	4·56	94·15	97·20	52·4

CASE

Date.	Diet.				Calories per kilo.	Urine.					
	Nitrogen	Fats	Carbohydrates	Fluids		Quantity	Sp. gr.	Total nitrogen	Urea	Uric acid	Ammonia
Period A.											
8— 9	19·72	124·87	248·87	1952	50·32	1350	1020	15·66	27·47	1·01	0·14
9—10	19·26	124·74	233·47	1952	48·53	1050	1022	12·93	21·88	0·85	0·19
10—11	17·16	118·88	233·47	1952	46·69	850	1021	12·02	20·57	0·77	0·23
11—12	17·40	118·26	244·71	1952	47·73	950	1024	13·17	22·33	0·93	—
Average.....	18·39	121·69	240·13	1952	48·32	1050	1022	13·45	23·06	0·89	0·19
Period B.											
15—16	21·33	130·24	249·94	2232	53·61	1000	1023	13·78	24·02	0·93	6·24
16—17	19·51	124·29	197·92	2176	—	940	1024	12·88	22·84	0·77	0·26
17—18	20·97	124·50	221·02	2120	—	950	1024	13·32	24·41	0·79	0·36
18—19	21·31	129·17	233·37	2204	51·12	850	1025	11·73	17·25	0·57	—
Average.....	20·78	127·05	225·56	2183	52·37	935	1024	12·93	22·13	0·76	0·29
Period C.											
22—23	35·12	176·05	260·12	2754	66·86	1300	1022	17·25	27·60	0·78	0·31
23—24	33·56	174·27	243·40	2642	—	1200	—	16·68	27·12	0·90	0·44
24—25	35·28	183·33	280·60	2754	—	950	1026	13·49	23·56	0·67	0·19
55—26	36·95	185·99	275·20	2754	70·46	1100	1020	13·30	19·80	0·88	—
Average.....	35·23	179·91	264·83	2726	68·66	1138	1023	15·18	24·52	0·81	0·31
Period D.											
29—30	40·79	220·16	323·92	3444	81·87	2250	1018	24·75	41·46	1·49	0·63
30—31	39·34	207·57	307·27	3164	77·75	880	1012	11·53	20·15	0·58	0·24
31— 1	40·22	208·48	278·87	3164	75·47	2190	1018	21·46	26·72	0·99	0·41
1— 2	40·22	196·90	278·97	3164	74·04	1370	1015	14·80	25·07	0·92	0·38
Average.....	40·14	208·38	297·26	3234	77·28	1673	1014	18·14	28·34	1·02	0·42

5.

Urine.						Fæces.				Absorbed per cent.		Weight, kilos.
P_2O_5	Chlorides	Sulphates				Quantity	Water per cent.	Nitrogen	Fats	Nitrogen	Fats	
		Total	Alkaline	Aromatic	Ratio, A : B							
1·44	5·40	2·44	2·17	0·27	8·0 : 1	185	80·15	1·70	8·38	91·43	93·29	53·4
1·76	5·27	2·36	2·13	0·23	9·3 : 1	196	89·32	0·96	4·77	95·02	96·18	53·8
1·35	3·10	1·80	1·61	0·19	8·3 : 1	159	78·21	1·10	7·97	90·68	93·29	53·6
1·34	4·47	2·06	1·85	0·21	8·8 : 1	59	76·11	0·64	3·22	96·32	97·29	53·4
1·47	4·56	2·17	1·94	0·23	8·4 : 1	150	80·95	1·10	6·09	93·36	95·01	53·6
1·78	3·65	1·99	1·74	0·25	7·0 : 1	100	76·13	1·21	2·22	94·33	98·29	51·9
1·60	4·14	1·92	1·74	0·18	9·6 : 1	100	76·13	1·21	2·22	93·79	98·21	—
1·33	4·33	2·11	1·85	0·26	7·1 : 1	73	69·63	1·12	2·06	94·66	98·38	—
1·49	3·10	1·70	1·43	0·22	6·7 : 1	72	69·63	1·10	2·03	94·84	98·42	52·9
1·55	3·81	1·93	1·70	0·23	7·4 : 1	86	72·38	1·16	2·13	94·41	98·33	52·4
1·29	6·39	2·18	1·75	0·43	4·1 : 1	347	81·01	4·48	6·59	87·24	96·26	53·9
0·68	5·28	2·41	2·10	0·31	6·8 : 1	114	77·04	1·78	2·61	94·69	98·50	—
1·64	4·18	2·16	1·90	0·26	6·1 : 1	166	91·53	0·95	1·60	97·31	99·13	—
1·32	5·28	2·06	1·75	0·31	5·7 : 1	300	77·17	4·65	6·85	87·42	96·26	54·0
0·94	5·26	2·21	1·88	0·33	5·7 : 1	232	79·44	2·97	4·41	91·67	97·54	54·0
1·37	9·47	3·99	3·36	0·63	5·3 : 1	138	76·28	2·16	4·25	94·71	98·07	54·0
0·79	2·73	1·97	1·73	0·24	7·2 : 1	138	77·72	2·16	4·25	94·51	97·95	54·0
1·75	8·32	3·33	2·92	0·41	7·1 : 1	163	75·39	2·64	5·22	93·44	97·49	54·5
1·64	6·17	2·31	2·05	0·26	7·9 : 1	144	71·49	2·71	5·34	93·24	97·29	54·1
1·39	6·67	2·90	2·52	0·38	6·6 : 1	146	77·72	2·41	4·77	93·93	97·70	54·2

CASE

Date.	Diet.				Calories per kilo.	Urine.					
	Nitrogen	Fats	Carbohydrates	Fluids		Quantity	Sp. gr.	Total nitrogen	Urea	Uric acid	Ammonia
Period A.											
8— 9	18·01	123·89	248 87	1896	42·49	980	1012	8·91	13·82	0·35	0·088
9—10	18·17	123·96	256·57	1924	42·77	950	1009	5·30	8·74	0·13	0·050
10—11	17·69	123·75	233·37	1896	41·11	1000	1010	6·89	12·71	0·38	0·092
11—12	15·96	119·82	241·17	1952	40·19	960	1010	6·05	10·85	0·22	0·099
Average.....	17·46	122·86	245·00	1917	41·64	973	1010	6·79	11·53	0·27	0·082
Period B.											
15—16	22·30	196·04	259·06	2120	54·87	1000	1011	8·18	13·47	0·28	0·10
16—17	23·03	198·16	259·06	2190	54·46	510	1020	6·63	11·80	0·26	0·10
17—18	19·22	175 99	234·36	2120	48·21	790	1010	5·14	9·80	0·22	0·09
18—19	20·52	191·66	243·66	2232	51·43	880	1014	7·53	12·66	0·28	—
Average.....	21·02	190·46	249·04	2166	52·24	795	1014	6·87	11·93	0·26	0·10
Period C.											
22—23	36·60	197·99	288·76	2866	60·78	1280	1014	11·90	21·38	0·37	0·13
23—24	36·91	209·63	284·37	2782	61·72	1430	1012	13·30	21·59	0·42	0·09
24—25	35·78	197·61	276·12	2782	59·52	930	1014	8·56	15·25	0·31	0·08
25—26	36·91	186·63	283·37	2782	58·02	880	1012	7·39	14·50	0·29	0·08
Average.....	36·55	197·72	283·16	2802	60·01	1130	1013	10·29	18·18	0·36	0·10
Period D.											
29—30	25·85	186·49	267·97	2670	52·64	1300	1015	12·74	21·45	0·68	0·09
30—31	26·01	185·56	275·67	2780	53·03	970	1014	9·12	14·16	0·39	0·11
31— 1	25·70	186·42	260·27	2670	51·78	1200	1012	9·84	—	0·35	0·13
1— 2	25·86	186·49	267·97	2780	52·33	1420	1012	12·78	20·87	0·51	0·22
Average.....	25·85	186·49	267·97	2725	52·45	1223	1013	11·12	18·83	0·48	0·14

6.

Urine.						Fæces.				Absorbed per cent.		
P_2O_5	Chlorides	Sulphates: Total	Sulphates: Alkaline	Sulphates: Aromatic	Sulphates: Ratio, A : B	Quantity	Water per cent.	Nitrogen	Fats	Nitrogen	Fats	Weight kilo
1·04	0·98	1·67	1·53	0·14	10·9 : 1	334	82·03	2·46	9·63	86·34	92·23	62·0
0·63	2·47	0·87	0·73	0·14	12·0 : 1	666	94·89	1·39	5·46	92·35	95·59	62·2
1·40	2·19	1·38	1·28	0·10	12·8 : 1	450	95·91	0·75	2·95	95·76	97·62	62·3
0·94	3·65	1·09	0·96	0·13	7·4 : 1	540	82·06	3·97	15·64	75·13	87·03	62·5
1·00	2·32	1·25	1·12	0·18	8·6 : 1	498	88·72	2·14	8·42	87·40	93·12	62·3
1·31	1·38	1·27	1·18	0·09	13·1 : 1	190	77·09	1·57	6·56	92·97	96·65	63·0
0·83	2·30	1·46	1·36	0·10	13·6 : 1	397	84·28	2·14	8·99	90·71	95·46	63·7
0·79	3·16	0·85	0·75	0·10	7·5 : 1	398	84·98	2·15	9·02	88·81	94·87	64·1
1·14	3·70	—	—	—	—	66	76·63	0·55	2·32	97·27	98·79	64·3
1·02	2·64	1·20	1·10	0·10	11·0 : 1	265	79·57	1·60	6·72	94·94	96·44	63·8
1·60	6·14	2·16	2·00	0·16	12·5 : 1	76	65·81	1·84	1·91	94·97	99·03	65·2
1·05	4·43	1·95	1·73	0·22	7·9 : 1	59	76·58	0·94	1·64	97·45	99·69	65·8
0·93	3·35	1·45	1·30	0·15	8·7 : 1	245	73·19	4·46	7·86	87·53	96·02	65·3
0·84	2·38	1·12	1·05	0·07	15·0 : 1	70	83·87	0·78	1·35	97·89	99·28	66·1
1·11	4·08	1·67	1·52	0·15	10·1 : 1	113	74·86	2·01	3·19	94·46	98·51	65·6
1·61	4·68	2·28	2·12	0·16	13·3 : 1	77	73·36	0·86	3·22	96·67	98·81	66·4
1·02	3·20	1·66	1·55	0·11	14·1 : 1	201	77·41	1·90	6·86	96·29	96·22	66·6
1·44	3·96	1·68	1·58	0·10	15·8 : 1	129	77·96	1·19	4·46	95·37	97·68	66·8
1·56	5·68	2·28	2·13	0·15	14·2 : 1	129	77·96	1·19	4·46	95·39	97·61	66·8
1·16	4·38	1·98	1·85	0·13	14·3 : 1	134	76·67	1·29	4·75	94·50	97·83	66·6

DISCUSSION.

Dr. BARDSWELL remarked that moderate quantities of food gave the best results. The diet in any given case was best fixed by considering the amount of weight the patient was below his maximum, and the range of the pyrexia as representing the activity of the disease. Further, if a patient put on one pound per week, the lungs did better than a more rapid increase. He was much opposed to "cramming."

THE PRESIDENT.—I think we must all admit that the paper shows an advance upon the former method of procedure; it dips more deeply into the chemistry of the living body than what we have been accustomed to. By estimating the ingoing and outgoing, and likewise taking the body-weight, we are enabled to form some opinion of what is going on within the body, and this paper decidedly gives us a step in that direction, and at the same time it is of practical importance with reference to the open air treatment of phthisis, which we know not only consists of living in the open air, but also in a copious supply of food.

Dr. CHAPMAN.—In regard to the diet chart shown by Dr. Bardswell I may point out that diet is calculated as a minimum diet other things taken being of the patient's own selection and counted extras, in other words, it is calculated so that if the patient took the items indicated alone he would be having a small diet; as a matter of fact, the other things he takes make it worth much more. For a man of ten stone this diet gives 35 calories per kilogramme, while with the extras it works out on the average at 50 calories.

Dr. HALE WHITE.—I have had some slight experience of this work because, by the kind help of Dr. Spriggs, I was able with him to publish in the 'Journal of Physiology' the account of similar observations during eight weeks on a patient who was undergoing the Weir Mitchell treatment. In the main, our results bore out the results which the authors have given us to-night. I do think, knowing how very great the labour of such work is, that the Society ought to be very grateful indeed for such a laborious series of observations. Those who have not done this work can form no adequate idea of the time and energy it requires. The patient observed by Dr. Spriggs and myself had a very large diet indeed, as large as I have ever known a Weir Mitchell patient take, and the results were approximately as follows:—She absorbed nearly all her fat, only about 3 per cent. of the undigested fat being found in the fæces. With regard to the nitrogen, at no period during the eight weeks did she

attain nitrogenous equilibrium. We found that the deficiency of nitrogen excreted was such that, even if all her increased weight had been proteid, which was very unlikely, she would still not have accounted for all the excess of nitrogen in the intake over the output. I believe the authors of to-night's paper also failed to obtain nitrogenous equilibrium, and that is a very interesting and striking fact, because we cannot but wonder what has become of it. One possible explanation is that the nitrogen is stored up in some other form than proteid, and another is that the amount of water in the tissues undergoes a diminution.

Dr. HORTON-SMITH.—I should like, sir, to ask whether the authors of this important paper can give us some simple rule for determining in a grave case how much food should be prescribed. Would it be correct in their opinion, for example, to say that a patient should be ordered as much food as he can possibly take, short of causing dyspepsia? If this should be so it would simplify matters considerably, for the difficulties, in private at least, of collecting the fæces and urine, and making an estimation of the total nitrogen, thereby obtaining an exact answer to the question, are obvious.

Dr. VAUGHAN HARLEY.—I quite agree with the President that we ought to be very grateful to the men who have carried out this work, because the amount of labour it entails is enormous, as any body who has done like work knows. The results show how science has progressed, and can be applied in medicine, as these experiments on metabolism constitute the application of physiology to pathology. I myself have found a loss of nitrogen frequently occur—more especially in Weir Mitchell cases—but I think it is generally due to cheating on the part of the patient, as, in normal individuals in the same metabolism experiments, the loss of nitrogen varies, rarely exceeding one gramme, and this is well within the margin of experimental error. The research, as we have heard, shows how forced feeding in normal individuals soon produces illness. In tubercular disease, on the other hand, you get a good effect; and these experiments show that, when you "cram" a patient by giving him 100 calories per kilo., the increase in weight is obtained at great expense to the patient, as, under these circumstances, the absorption of proteids is very low, and the increase in nitrogen rest in the urine high, showing how the metabolism itself is strained. If, however, you decrease the diet to 50 or 60 calories per kilo, you get a maximum absorption with a minimum amount of labour, and the patient makes steady progress day by day, showing that this is what you ought to aim at. To calculate the right number of calories per kilo., you ought to take not the actual weight of the patient, but his

weight when in health, and the number of calories per kilo. can be reduced as the patient improves.

Dr. GOODBODY.—With regard to the difficulty of obtaining nitrogenous equilibrium I may say that these experiments lasted four weeks, with six patients under observation, and the results in one patient were unsatisfactory. We had altogether twenty-two different observations, and in three of them we succeeded in getting the patient practically to nitrogenous equilibrium, *i. e.* we could account to within one gramme of the nitrogen given in the food. With regard to Dr. Hale White's remarks as to the difficulty of accounting for the nitrogen, it appears to me that one possible explanation is that the nitrogen as stored up in the connective-tissue cells; when fat is deposited in these cells a large portion of the fat is dead, only a very small portion round the nucleus remaining active. Although there may not be such a very great increase in weight, why should not this dead cellular tissue disappear and active cells take their place, containing a much larger quantity of nitrogen? In this connection, as I mentioned in the paper, there was a large increase of weight in phthisical patients with forced feeding, but all this weight was lost within three weeks, and I can vouch for it that I felt a great deal better when the extra weight had disappeared. With regard to Dr. Horton-Smith's question, the estimate of the urea by the hydrobromate method will give a certain amount of information provided the amount of nitrogen in the food is known, but the best method I know of at present is that which gives a trustworthy estimate of the nitrogen in the urine and fæces.

ON TWO CASES

BEARING UPON THE

QUESTION OF THE LIMITATIONS OF ENTERECTOMY

BY

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THE two cases now to be recorded appear to have some value, assisting us, as they may, taken with others, to form conclusions in regard to the limitations of enterectomy, which can only be settled by experience.

The first bears upon the question whether this delicate and difficult operation, which demands a very full measure of reparative power on the part of the patient, ought to be undertaken at all in the presence of marked glycosuria. This condition is well known to exercise in various ways a most depressing influence upon all the vital processes, and might be assumed for that reason (perhaps too readily) to absolutely contra-indicate an operation, such as the removal of part of the bowel and end-to-end anastomosis of the same.

The second, in which five and a half feet of small

intestine were removed for gangrene in a woman of seventy-six, raises the question whether advanced age is of itself a barrier to the removal of large tracts of the intestinal canal with end-to-end anastomosis. It also gives some hints as to the extent to which such excision may be carried, and the effects on assimilation of removal of large portions of the small bowel.

Both cases having been followed by complete recovery, we are in a better position now to argue from experience than before.

Case 1.—The first case is as follows:—Mrs. M—, aged 58, was admitted into University College Hospital on October 3rd, 1900, under the care of Dr. G. V. Poore. She complained at this time of great pain above the umbilicus and obstinate constipation. She was known to suffer from diabetes, and later was found to have 6·6 per cent. of sugar in the urine. The pain had begun eight months ago, and she was obliged to remain in bed from the middle of May to the end of June, 1900. After this she was advised by her medical attendant, Dr. Baldwin, to go to the sea-side for three weeks. Here she improved on a diet chiefly of fish. Since returning home the pain has been very intense, especially after solid food. She has usually been sick half to one hour after food, but has had no hæmatemesis, except on one occasion three weeks ago. Three weeks before admission she could not keep down even soda water and milk. She has always been constipated, and states that drugs had no effect upon this condition. Three weeks before admission she had "coffee-ground" vomiting. Her aspect is that of a fairly healthy woman, and in spite of having lost 2 st. 6 lbs. during the last six months she looks fairly nourished. She has no appetite. The abdomen, on inspection, looked like that of a healthy woman who had borne many children (ten). There was tenderness above and to the left of the umbilicus, and here an oblong tumour could be felt; it lay across the abdomen, and was sausage-shaped and moderately

firm and moveable; otherwise the abdominal contents showed nothing abnormal. The urine was acid, sp. gr. 1040, contained no albumen, but gave the reaction of sugar. When Dr. Poore kindly asked me to see the patient with him we agreed to distend the stomach with air, and then after evacuating it to inflate the colon. When the stomach was distended the tumour was a little less evident, but was otherwise unaltered. On distending the colon, however, the tumour was pushed to the right iliac fossa and reduced in size. From this we argued that it was probably seated in the transverse colon, and was associated with more or less intussusception of a ring-like growth of carcinoma into the distal portion of the bowel.

The patient being in fair condition, except for the glycosuria, it was determined to attempt removal of the growth.

The preparation for operation consisted in clearing out the descending and transverse colon by copious enemata, drugs having failed. Codeine phosphate in one-grain doses was given three times daily hypodermically for the diabetes, and bismuth carbonate gr. x ter die as an intestinal antiseptic.

Operation (October 25th, 1900).—The abdomen was opened in the middle line by a three-inch incision, branched below to include the navel, which was excised. The mass was found to the right of this opening, and on being lifted out with ease was seen to be an annular mass of carcinoma, producing a very tight stricture of the colon. The bowel above contained hard scybala, and was much hypertrophied; below the mass it was empty, dilated, and thin-walled. There did not appear to be any glandular infection, but there were a considerable number of adhesions, with portions of the omentum round the growth. The latter was now separated from the omentum after ligature in several pieces. The bowel was then closed by several pairs of Doyen's forceps above and below the growth, and the middle portion of the colon was cut clean out with scissors, which were also employed to cut across the mesocolon about an inch and a half from the portion

removed, in the centre of which was the annular cancerous stricture. The portion of colon removed measured, in the contracted condition, four and a half inches, about one inch of this being taken up by the growth.

The ends of the divided bowel were now brought together after being cleansed, and were sutured end to end in the usual manner with fine silk stitches in two rows, a deep and superficial. Then the gap in the mesocolon was closed by a continuous silk suture. When the clamps were now removed the continuity of the bowel appeared to be satisfactory, and the abdominal wound was united by silk stitches passing through all the structures of the edges, and without any drainage.

The patient bore the difficult and prolonged operation particularly well, and soon recovered from the anæsthetic. She expressed herself as at last free from the severe pain from which she had suffered for months. The temperature remained below 100° for the first nine days, during which she steadily improved There was no vomiting, except a mouthful soon after the operation. Feeding by the rectum was kept up for four days, and small quantities of fluid were given by mouth from the second day onwards. Morphia was given, at first two or three times daily, but on the third day I began to administer codeine phosphate in one grain doses hypodermically three times daily, on account of the sugar in the urine, which was shown on the fourth day to amount to 6·6 per cent. From this day it steadily declined in amount, until on the ninth day it was only 2 per cent. It diminished now still more rapidly when the codeine in the same amount was given by the mouth until the thirteenth day, when it disappeared altogether, only to reappear, once to the amount of 2·8 per cent. on the seventeenth day, when it was found that the patient had surreptitiously eaten some sugar and also grapes. After this sugar was either totally absent or only found in a mere trace until the end of convalescence.

For the first ten days the original gauze dressings were

not removed, as the temperature had remained practically normal, and the patient's abdomen appeared perfectly quiet, except for some flatulence. On the tenth day, when the dressings were taken off for the first time, it was evident that some suppuration had taken place. The stitches were cutting and the edges were somewhat swollen and red; a few bubbles of gas escaped also with the pus from the upper stitch holes. The temperature, however, was only 99°, and the local and general condition otherwise very good. The wound was supported by American rubber plaster. This day an oil enema was given with only a slight result; but much flatus was passed subsequently. The next morning, at the dressing, it was quite clear that a small amount of fæces was escaping from the upper stitch holes, and this increased for a few days and then began to lessen. After the first two stools on the nineteenth day after operation, which were very copious, the discharge of fæces from the fistula became insignificant, until on the twenty-seventh day it ceased altogether for a week. On the thirty-second day there was some swelling and redness at the lower end of the wound, and the next day a slough was seen protruding, which on being pulled on was about the size of the little finger, and was seen clearly to consist of a piece of omentum or mesentery with one or two silk stitches attached. There had been a smaller slough of the same kind extracted some days earlier, but no record was made of it. All this time the patient's condition was excellent. The bowels acted regularly with or without enemata, and abundant liquid and solid food was taken.

Two days after the discharge of the slough above mentioned there was a trace of thin fæces on the dressing, but the wound healed rapidly, and was almost definitively closed on the day the patient left hospital, only a tiny point of granulation remaining. This was on January 13th, 1901.

The portion of colon removed is here exhibited. It is now four and a half inches long, and shows the hyper-

trophy of the afferent portions and the dilatation and thinning of the lower portion. In the middle lies the ring of carcinoma, which only admitted the passage of the tip of the little finger before it was slit up. Under the microscope the growth was seen to be an ordinary columnar epithelioma.

The chief interest of this case appears to me to centre round the fact that this patient had for years been a diabetic, and at the time of the operation was getting rid of 6·6 per cent. of sugar in her urine, and was growing thinner. Hitherto such a state of things has generally been held to contra-indicate most severe operations. But surgery has altered much with the introduction of aseptic conditions, and it is possible we may consequently have to revise our notions still further in regard to the possibilities of repair in diabetic patients, and with them our practice. Such cases as the foregoing help us somewhat in forming conclusions on this point. Personally I can only remember three cases in which I have been called upon to do *abdominal* operations on diabetic patients. The first was one of carcinoma of the rectum with complete obstruction, for which colotomy was necessary. Here there was no repair in the wound, and the patient died comatose. The next was a radical cure of an umbilical hernia where the sugar was overlooked before operation. Here, as I expected when the sugar was found the day after operation, the repair was bad, and the wound broke down, and only very slowly healed. And although the patient appeared well generally throughout, I was very anxious until he left hospital in good health.

In the present case I was, to some extent, encouraged by the last as showing that union of the abdominal wall, at all events, could take place in a diabetic. But there are very few cases, so far as I know, in which enterectomies have been done in this condition, and there was little evidence to show how repair *of the gut* would take place in a diabetic patient. It appeared, however, probable that if other tissues can heal in the presence of

sugar in the blood, the peritoneum, if kept clean, could with its wonderful reparative power do so too. I confess I expected more or less of a fæcal fistula in this case. This is very common in enterectomies of the large intestine under ordinary conditions, and would be more likely where sugar was present. But in spite of this it appeared proper to face the risks of operation in view of the almost complete obstruction and the inevitable death which must soon follow if nothing was done.

The slight sloughing of the omentum and mesentery in this case is new to me. I have tied these structures in many operations, but until now have never seen any evidence of necrosis in them. This, I think, can be fairly ascribed to the lowering of their vitality, due to the presence of sugar in the blood.

Case 2.—The second case is that of a feeble old woman aged 76, admitted into University College Hospital on January 10th, 1901. She had always enjoyed good health, but in 1870 had undergone ovariotomy. She had had no children. For two years she had had a large ventral hernia in the ovariotomy scar. On January 8th and 9th she had not felt well, and complained of some pain in the abdomen, but was not sick. At 10 a.m. on January 10th the patient was seized with severe pain in the abdomen, and vomited the contents of the stomach slightly bile-stained. The hernial tumour was tender and more swollen than usual. There was no more sickness, and no motion or flatus was passed. At 11.20 on January 10th she was seen by Dr. Rainsford Gill, of King Henry's Road, who states in a letter that he was called to see her for what appeared to be a fainting attack. She then appeared in but little distress. Two hours later she had vomited, and had another attack of faintness. The vomited matter contained masses of undigested bacon. He again saw her in about an hour, and she "then complained *only* of epigastric pain—*none* in the lump, which she mentioned was as usual. I had my doubts, and sent

her down to hospital; the doubt only occurring because manipulation seemed to increase the epigastric pain, and I thought it must mean involved omentum."

State on admission described as follows:—Feeble woman, with intermittent pulse of 108; face pinched; tongue moist; condition, but for age, good.

There is a lobulated median ventral hernia five inches in diameter, extending from umbilicus to pubes. The front of the sac has the scar of an ovariotomy in it. The tumour is tense, dull, not tender, and shows no impulse on coughing. There is definite fluctuation and thrill across it.

When I first saw the patient at 10 p.m., and examined the mass under an anæsthetic, some of the contents of the sac returned easily and at once, and the whole pelvis was found to be full up with very hard masses, discovered later on opening the abdomen to be fibroids of the uterus probably calcified.

Operation.—I immediately opened the abdomen through the old scar, and about a pint of dirty blood-stained fluid with a fishy odour gushed out. A loop of blackened small intestine was now seen of about three feet in length, strangulated through the omentum. The gut had not entirely lost its lustre, but was very foul, and distended tightly with dark blood-stained fluid. The peritoneum was not cracked, but hæmorrhages existed beneath it in several places, and a few of the subperitoneal venules were thrombosed. The extremely foul and fishy odour of the gut and fluid around it determined me to remove it, as its recovery seemed hopeless. I therefore cut away five feet and a half of the bowel, and anastomosed end to end as rapidly as possible. The time taken for this part of the operation was forty-four minutes, the whole operation to the last stitch requiring sixty-three minutes. During the operation, which was well borne, ℥xij of normal saline solution were slowly injected subcutaneously. The whole of the lower part of the abdomen was filled up with very hard fibroids of the uterus which reduced the amount of space for working very much.

The 'Surgical Registrar's Report' next morning on the portion of gut removed is as follows:

Parts removed.—"Five and a half feet of small intestine. Three inches from the lower end is the seat of the distal constriction. The gut at this point suddenly becomes intensely congested and hæmorrhagic, of a purple-black colour, and its walls are thickened with intense œdema. At the time of operation there was a definite groove at this spot, which has now disappeared, after lying in weak spirit for twelve hours. On tracing the gut upwards from this point, the first three feet are all intensely congested, thickened, and œdematous, but the changes become less marked above, and the upper two feet, though now only pale and œdematous, were congested at the time of operation.

"There is no groove or sudden change in the pathological appearances to mark the seat of any constriction of the proximal loop of gut, the congestion and œdema becoming gradually less when followed up the coil of gut.

"On slitting up the gut the mucous membrane of the lowest three feet has a deep purple-black colour, and the valvulæ conniventes are so swollen, discoloured, and pulpy-looking that it is difficult to say whether any ulceration exists.

"After lying some days in weak formalin the parts merely congested became paler, and revealed three large patches in the last eighteen inches of gut, where the mucosa was hæmorrhagic, partly gangrenous, and superficially eroded. Each patch involved the whole circumference for about three inches, and the lowest one, where the changes were most marked, had a definite, abrupt, linear lower border, marking the seat of the distal constriction.

"In the next foot of gut above there were two similar but smaller patches of mucous hæmorrhage and erosion, only involving a part of the circumference of the bowel for about one inch by half an inch."

January 11th.—During the night the patient had an enema of hot saline solution with ℥ss of brandy, followed in two hours by a nutrient suppository. She also had ℥j of albumen water every two hours. There was only slight sickness once. The temperature this morning was 100°; pulse 120, intermitting 1 in 8; respiration 30. There was slight distension, but no pain or tenderness, and patient passed water without the catheter. Her colour was good. No flatus.

The treatment consisted in nutrient suppositories every four hours, with saline injections *per rectum* every alternate four hours. She also had ℥j of albumen water with ʒj of brandy every two hours by the mouth. She also took gr. xx of Bismuth. Carb. and ♏ij of Liq. Strych. This day the temperature rose to 101°, but soon fell to below 100°. Fearing trouble in the lungs in an old person, I ordered that she should at once be put in a sitting position and kept so throughout, except for a few hours, when she was to sleep in the horizontal position.

There is little now to record except uninterrupted convalescence. The food was rapidly increased, until soon the patient was taking brandy ℥ix, albumen water ℥xxiv, Benger's Food ℥viij, and later eggs, pounded meat, and fish. My chief anxiety was about the bowels. These acted twice on the fourth day, three times on the fifth day, four times on the sixth day, and five times on the seventh day, which led me to fear septic catarrhal enteritis. This is not to be wondered at when we remember the state of the bowel above the constriction. The diarrhœa was checked, however, by a few doses of ♏v of Liq. Opii, and there was no further trouble until the twelfth day, when there was another looseness of the bowels. There was just a trace of bronchitis, but never to cause alarm, and it was kept under by rubbing the back, the sitting position, and wool packing. In order the better to combat all lung trouble I thought it well to let the patient sit up in an arm-chair on the sixth day by the fire for some time. This seemed to produce a good

effect. The wound was not dressed until the tenth day, when primary union was found. A strip of collodion gauze was put over the wound, and the whole abdomen was supported with rubber plaster.

Returning now to the first of these two cases, I need hardly remind this Society that important papers have been published comparatively recently in its 'Transactions,' tending to show that, under the improved conditions of antiseptic surgery, the prospect of operations for diabetic gangrene are now by no means so gloomy as formerly. But it must not be forgotten that only thirty-five years ago the Surgical Society of Paris debated the question whether *any operations at all* ought to be performed on diabetic patients, and came to the general conclusion that only those conditions which without an operation would inevitably end in death should be dealt with,—as, for instance, by tracheotomy or herniotomy. And many present on that occasion still maintained that no operation, even the smallest, should be done in the presence of glycosuria. But though it has been since shown that amputations for diabetic gangrene have been performed with a fair measure of success, we have still but little evidence as to how operations upon the intestines are borne in the presence of glycosuria. This case, then, appears to offer some encouragement.

As far as we know from recent investigation the way in which sugar in the blood and tissues operates in producing that lowering of vitality which finds its grosser expression in gangrene of the extremities, and its lesser in more limited necrotic changes in the lungs, intestinal and renal epithelium, is somewhat as follows:

The derivatives of altered tissue change due to glycosuria, such as acetone, acetic, lactic, β-oxybutyric, and oxalic acids, injure the tissues, and make them more vulnerable to infection. They are the source[1] of occasional necroses of internal organs, of premature angiosclerosis,

[1] Grossman, 'Ueber Gangrän bei Diabetes mellitus,' p. 127.

and, in combination with increased destruction of albumen and diminished repair, are the origin of precocious senility.

All recent authors have found extensive arterial disease in diabetes.

Degeneratve neuritis is a secondary result of this defective blood-supply to the nervous system due to angiosclerosis.

There are, then, two forms of extreme lowering of vitality due to glycosuria, often producing necrosis—(*a*) that due to angiosclerosis and thrombosis, and (*b*) that due to inflammatory processes started by virulent forms of bacteria in weakened tissues.

Further, it has been shown that the amount of sugar which is found in the blood and tissues of diabetic patients corresponds pretty nearly with the amount which is found by bacteriologists to be most favourable to the growth of pathogenic organisms on cultivation media. Dr. Pavy pointed out long ago that the blood of diabetics contains about on an average 0·6 to 0·5 per cent. of sugar, and many experimenters have found that this is the best percentage of sugar for agar-agar or bouillon if the organisms are to grow at their very best, while a higher percentage either inhibits their growth or reduces their virulence.

It would follow from this that, after all, the chief danger to wounds in diabetes is sepsis, and that with the avoidance of this even delicate reparative processes, such as the soldering up of intestinal wounds, may be hoped for. The other forms of lowered vitality would remain, of course, as well as that due to chloroform narcosis, and have to be faced. But we can avoid violence to the tissues by delicate manipulation, and can now spare them the further devitalising effects of strong chemical germicides.

The only reference to changes in the intestines found in cases of diabetes made by Dr. Saundby, in Allbutt's 'System of Medicine,' is as follows :

Intestines.—"These share in the congestion and catarrh which are found in the stomach; hæmorrhages may be present in the duodenum. The large intestine is generally filled with hardened fæces, and occasionally shows dysenteric inflammation or desquamation of its epithelial lining."

Again in his "Summary:"

"Diabetes is a disease which has so profound an influence upon the general nutrition of the body, that it tends to produce structural alterations in the various organs, which are for the most part of a secondary and degenerative character."

Out of the many features of interest in Case 2, that of the removal of five and a half feet of small intestine in a feeble old woman of seventy-six for gangrene, I will only specially allude here to three. First, that the advanced age appeared to be no barrier to the most perfect repair, for everything apparently healed as it might have done in a patient fifty years younger. Next, that so far we have no evidence that in her case the withdrawal of so large a part of the secreting surface of the small intestine has had any injurious effect upon the system. Digestion seems now very good, and the motions appear normal.

Finally, this case *suggests* that in some cases of internal strangulation with damaged, paralysed bowel, distended with intensely septic products, but not actually gangrenous, it might on the whole involve less risk to cut away all the damaged portion with its contents than to return it to the abdomen with or without evacuation after its release from strangulation. How often have we seen such cases die of intestinal sepsis or peritonitis many days after the release of a constriction and with a healed wound, the bowel being found after death still flaccid and discoloured, though in no way perforated!

Some undoubtedly recover, but often after violent enteritis, and some only to fall victims to other forms of obstruction set up by adhesions.

I may add that, just before the first of these cases was

admitted to the wards, I had to resect in another case 37 inches of small intestine which was all matted together and kinked, causing almost fatal obstruction. In this case I had operated on a strangulated femoral hernia four months before. And though the discoloured loop was far short of gangrene, and the usual wound healed perfectly by first intention, admitting of the patient leaving hospital on the sixteenth day, two very severe attacks of acute obstruction, each nearly fatal, followed with intervals of about a month. And when in October I opened the abdomen to see the cause, the knuckle of intestine which had been in the hernia was found so sharply kinked and held down by matting adhesions, that it was a marvel that the patient had so long survived. Fortunately the removal of 3 feet 1 inch of the damaged intestine with end-to-end union was followed by complete relief, but I now think it would have been better to have done it in the first operation.

APPENDIX

The consideration of the second of the above cases could hardly be regarded as complete without some references to those other extensive resections of the intestine which have been published up to the present.

Taking 1 metre (39·5 inches) as a minimum limit, I have been able, with the help of various publications (see below), to collect twenty-seven successful resections of intestine exclusive of my own. These range themselves as follows:

Between	1	and	2	metres	.	.	21	cases.
„	2	„	3	„	.	.	5	„
„	3	„	4	„	.	.	2	„
							27	„

The amount removed actually ranged in this list between 100 cm. (3 feet 3½ inches) and 300 cm., or 10

feet 10½ inches. This largest amount was removed from a boy of eight, whose condition a year later showed no evidence that the loss of so much of his small intestine had unfavourably affected his health. Of the others it can only be said that those who had lost under 1½ metres (4 feet 10¾ inches) appeared to suffer nothing permanently from the operation. Of the seven, including my own, in which between 1½ and 2 metres had been sacrificed, two showed some disturbance of the assimilative process. My own case, the old woman of seventy-six (66 inches), has had, on three occasions, slight diarrhœa to the extent of one or two loose stools, but otherwise appears to be in the best of health, and to have put on flesh. In the other (Schlatter's), where 192 cm. or 6 feet 4 inches were removed for strangulation in a healthy man of twenty-three, the patient was soon able to take any kind of food, and increased largely in weight while in hospital. A year after he was found to have lost 3 kilos., and to be unable for prolonged physical exertion. In the five cases in which between 2 and 3 metres had been removed, diarrhœa is noted in three when the diet was not regulated; otherwise the patients were well. In the fourth case, a man of twenty-two, from whom 202 cm. of small intestine were removed, there is no record of any intestinal fault; the other was quite well until death two and a half years later. In the two cases in which respectively 310 cm. and 330 cm. of small intestine were resected, the condition of the patients at the end of a year showed no loss of weight; but in the first, a man of sixty, an analysis of the excreta showed that assimilation was not perfect, but was made up for by the amount taken.

In only two of all these cases was a careful analysis made of the excreta after the operation. In Fantino's case (310 cm.) assimilation was obviously below normal. This was indicated by the rapid appearance in the stools of aliments which could be recognised; and besides, the bowels acted more frequently than normal. Moreover, a chemical analysis showed that the motions were richer

in nitrogen, fats, and water than normal, but in spite of this the weight increased.

In Schlatter's case practically the same results were arrived at by an analysis of the excreta.

From all this it would appear that about two metres of small intestine, say six feet, may be removed without any serious damage to the subsequent assimilative powers. But I think no one can study these cases without arriving at the conclusion that in this length we have probably arrived nearly at the limit of safe resection of the small intestine. And I feel glad that I had some recollection of having read some of these conclusions somewhere when I was suddenly called at night to operate on this case. It led me to roughly measure what I was about to excise by passing it a foot at a time through my fingers before fixing on the spots to divide the bowel. I remembered, I believe, Senn's conclusion that not more than one third of the whole of the small gut should be taken away; and though the upper part of the bowel at the spot selected for division was still œdematous and hæmorrhagic, I determined to keep within these bounds. It is true that Senn's conclusions were based upon his experiments upon dogs, which might be misleading. It is true, as I have since read, that Trzebecki's experiments on dogs led him to believe that one half of the small intestine might be safely excised in man, and that Monari, after a series of similar experiments, arrived at the result that dogs will bear the loss of seven eighths of their small intestine, and that probably the human being might be deprived safely of two thirds. It is also true that a boy eight years old has actually lived and grown strong after forfeiting 10 feet 10 inches of small intestine. But the danger of arguing from experiments on dogs or from one or two cases affecting the human subject is clearly suggested by some of these cases, which appear to come perilously near the justifiable limit. And the great value of accurate clinical records is thereby to my mind abundantly shown where abstruse physiological problems are involved. It seems

probable, from experiment and observation, that in younger patients who survive the operation a compensatory hypertrophy may take place in the small bowel left behind, which may make up for the loss. It seems also to be suggested that the resection is better tolerated the lower down the intestinal tract it is done.

Cases of Resection of Bowel to the extent of more than One Metre which were Successful.

1. Hahn.—Excised 80 cm. small gut, 20 cm. of large, in a man aged 38 years. No disturbance of assimilation. Cause of trouble, volvulus.

2. Budberg.—Koch excised 110 cm. for gangrenous inguinal hernia. Recovery. M. aged 38.

3. Budberg.—Koch excised 107 cm. of colon for volvulus. M. aged 42.

4. Troje.—Excised 115 cm. small intestine for tuberculous strictures. F. aged 25.

5. Schlange.—Excised 135 cm. of ileum for gangrene, due to strangulation. No disturbance of nutrition. F. aged 42.

6. Kocher.—Excised 160 cm. of ileum for gangrenous inguinal hernia. M. aged 57. No disturbance of nutrition.

7. Kukula.—Excised 110 cm. of the jejunum for fæcal fistula. F. aged 42. Two years later no intestinal disturbance. Health excellent.

8. Trendelenburg.—Excised 85 cm. of ileum and 20 of large intestine for fæcal fistula. M. aged 27. Six months later perfect health.

9.—Kocher.—Excised 141 cm. ileum for intussusception of lower part of bowel. M. aged 20. Ultimate result unknown.

10. Budberg.—Koch excised 175 cm. of the ileum with cæcum and v. appendix for strangulated scrotal hernia. No disturbance. M. aged 36.

11. Wullstein.—Excised 175 cm. ileum for strangulated hernia. M. aged (?). Ultimate result not given.

12. Schwalbach.—Excised 183 cm. ileum for strangulation. F. (?). Ultimate result not known.

13. Hinterstoisser.—Excised 186 cm. of ileum and partly jejunum. F. aged 36. No disturbance.

14. Elliott.—Excised 124 cm. for gangrene due to mesenteric thrombosis. Man aged 25. Good health two years later.

15. Roux.—Excised 124 cm. for a lipoma. Recovery.

16. Canthorn.—Excised 109 cm. for sarcoma of mesentery. Aged 49. Recovery; died four months later from obstruction by Murphy's button.

17. Maston.—Excised 112 cm. for sarcoma of mesentery. Recovered, but died five months later from perforation due to Murphy's button.

18. Trombetta.—Excised 110 cm. F. aged 40. Recovered.

19. Barker.—Excised 165 cm. for gangrene due to strangulation through hole in mesentery, "end-to-end" anastomosis. Woman aged 76. Recovery, slight diarrhœa at first.[1]

20. Schlatter.—Excised 192 cm. for gangrene due to wound and prolapse. The patient was aged 23. During stay in hospital he ate anything and increased in weight. A year after had gone back in weight 3 kilos., and could not work as hard as before.

Cases of Resection of Bowel to the extent of over Two Metres which were Successful. Quoted in papers by Shepherd and by Dreesmann.

1. Kœberle.—205 cm. of small intestine for strictures. F. aged 22. No disturbance of assimilation.

2. Kocher.—208 cm. of small intestine for railway injury. Diarrhœa when incautious about diet. M. aged (?).

[1] Remained well with regular motions, and is in good health now a year after operation.

3. Dreesmann.—215 cm. ileum for gangrene. Aged 37. Diarrhœa easily produced by errors in diet.

4. Shepherd.—234 cm. ileum adherent to tumour. Aged 28. Frequent loose stools, but gained 40 lbs.

5. Kukula.—Excised with a mesenterical tumour 237 cm. of ileum. F. aged 38. For two and a half years perfect health, then death from recurrence of tumour.

Cases of Resection of Bowel over Three Metres which were Successful.

1. Fantino.—310 cm. ileum for gangrene. Aged 60. No emaciation at end of a year.

2. Ruggi.—330 cm. of small intestine for peritonitis. Boy aged 8 years. Quite well a year later.

References to the Effect of Removal of Large Tracts of the Small Intestine.

Senn.—'Experimental Contributions to Intestinal Surgery,' 1892.

Trzebecki.—'Langenbeck's Archiv,' Bd. xlviii, p. 54.

Monari.—'Beiträge z. klin. Chir.,' Bd. xvi, Hft. 2.

Dreesmann.—'Berliner klin. Wochenschrift,' 1899, No. 16.

Shepherd.—'Brit. Med. Journ.,' 1896, p. 966.

Kukula.—'Langenbeck's Archiv,' Bd. lx, Hft. 4.

Schlatter.—'Lancet,' 1900, January 27th, p. 217.

Fantino.—'Centralb. f. klin. Chirurgie,' 1896, p. 614.

DISCUSSION.

The PRESIDENT.—Diabetes has been brought into the question before the Society this evening, and I have been asked to speak upon the matter. To this I respond, although I had not originally intended to take part in the discussion. The surgeon, it seems, regards his position in relation to operative treatment in diabetes differently now from what he did formerly. We can scarcely think that surgeons of former times were wrong in the view they then took, nor can we think that the surgeon of the present day is wrong in the view that he now entertains. To what, it may be asked, is the difference attributable? We cannot, I think, attribute it to any alteration in the character of the disease, but may it not be that the physician's measures of treatment are more efficacious now than formerly in controlling it, thus placing the patient in a better constitutional state? If we have the alimentary form of diabetes to deal with, that is, diabetes where the sugar abnormally present in the system is derived solely from the food, the system can be kept free from such sugar by appropriate dietetic management, and whilst this is effected the diabetic patient is to all intents and purposes in as good a state of health as an ordinary person. The sugar reaching the urine in this form of the complaint is the result of faulty assimilation of the food carbohydrates. Thus sugar is permitted to reach the blood of the general circulation, and in proportion as it does so, so is the extent of deviation from the natural state, and so the impairment of the health. Under normal circumstances the carbohydrates of the food are assimilated and prevented reaching the system as sugar, which thence fails to show itself in the urine. In diabetes, on the other hand, the assimilative power is at fault to varying extent in different cases. In one instance there may only be a slight impairment, when the patient can take a considerable amount of carbohydrate without sugar getting into his system or urine. In other cases the assimilative power may be more or less small, and then only a correspondingly small amount of carbohydrate can be taken without sugar getting into the system. The issue depends upon the amount of assimilative power existing. Keep the carbohydrate within the assimilative power, and you thus keep the patient in a right state. Probably the patient's case referred to in the paper belonged to the category in which this could be effected, and in which experience shows that operative measures can be undertaken with success. There is, however, another form of the disease, a form where the sugar is not only derived from faulty assimilation of the food carbohydrates, but also in part from an abnormal breaking down of the tissues. This form is

not controllable by diet in the same way as the other. You may reduce the sugar, but you cannot entirely remove it, and the patient with this form of diabetes cannot be placed in the same satisfactory condition of health as the one who is suffering from the alimentary form only of the disease. Moreover, such a patient is in danger of at any time being rapidly carried off by a process of auto-intoxication, arising from the abnormal tissue breaking down process being attended with the production of toxic agents which lead to the occurrence of diabetic coma, a danger to which patients with the alimentary form of diabetes are not exposed. Patients with the twofold source of the sugar may be said to be suffering from the "composite" form of the disease, and it is in this class of case that the great liability to an unfavourable issue exists in connection with surgical operations.

Sir THOMAS SMITH.—We are greatly indebted to you, sir, for the information you have volunteered. Even in the other form of diabetes I have witnessed your success in reducing the sugar so as to make an operation a reasonable proceeding. How dangerous a slight injury may be in a patient in whom the sugar is under no sort of control I may illustrate by the case of a gentleman who came to me with a small trouble near his shoulder, where there was a minute tract under or rather in the skin so small that only the finest probe could pass. I laid it open, a quite trifling operation, and he left by train for Leamington, where he was found unconscious in the carriage lying in a pool of blood. In another case, a gentleman, who was supposed to be in good health, aged 40, gave a dinner party to his friends in Paris, and in opening an oyster, scratched his finger, giving issue to a little blood. That night he had a great deal of pain in his hand, but set out the next day to return to England, but was obliged to stop at Boulogne. When I saw him two days later there was gangrene of all the extremities and patches of gangrene in other parts of the body, and he quickly died. We often have to amputate for diabetic gangrene, and that not unfrequently before it is possible to wait for medical treatment, so that certainly there is something in modern surgery to account for the greater immunity of these patients.

Sir DYCE DUCKWORTH.—We know that the presence of sugar in the urine of elderly people is of much less consequence than in early life. We are glad, sir, to have your lucid definition of the two varieties of diabetes. We have, I think, learned to recognise that the two classes of cases may pass one into the other, while some cases are on the borderland. In practice, it is not always possible to distinguish between the two, and it may be necessary to operate before one can treat the condition. I think it would be well for the surgeons to recognise that the

patient whose urine contains sugar is almost certainly a vulnerable subject, and that operations on such persons present special dangers. Although in these days of clean surgery these risks may be minimised, I know of cases in which, in spite of every precaution, disastrous results have accrued, due, probably, to reinforced disturbance of metabolism resulting in coma and death.

Mr. A. Barker.—I fully admit our indebtedness to the physicians in preparing these patients for operation, but I would point out this particular patient was not really under the control of the physicians, because she had to be operated upon for almost acute intestinal obstruction at a time when the amount of sugar had not been reduced. The specific gravity of the urine was 1040, and it contained 6·6 per cent. of sugar. This condition lasted through the first ten days, in fact, throughout the period within which surgeons reckon upon their patient's recovery or death after an enterectomy. During all that time there was abundant sugar in the urine. It was not even materially reduced until the ninth day, and that is why I brought the case forward. In respect of the second case, I think we very nearly reached the limit of the amount of intestine that can be removed without serious effects. I have seen the patient to-day, she is passing her motions quite regularly, and presents every appearance of health, in spite of the advanced age of 76.

ON A CASE

OF

INTESTINAL INTOXICATION DUE TO APPENDICITIS

WITHOUT LOCAL SYMPTOMS

BY

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Received May 8th—Read May 14th, 1901.

THE case to be recorded illustrates an interesting combination of symptoms and pathological association, and is worthy of record from its unusual character.

The facts of the case are as follows.

A gentleman aged 50, under the care of Dr. C. D. B. Hale, was brought to see me, with symptoms pointing to an intestinal intoxication. The patient had never suffered from any recent serious illness. He had had slight eczema, which was considered gouty in origin, and had suffered from scarlet fever at the age of four.

He had been fishing in Norway in the summer of 1899. On the voyage home, which was stormy, he was sea-sick, and suffered somewhat from looseness of the bowels.

The symptoms from this time to the date (eight weeks later) at which I saw him were chiefly referable to the intestinal tract. There was no indigestion of food, but there was gradual loss of appetite, with, finally, complete anorexia. There was a bad taste in the mouth, and a dry tongue, with a greatly deficient secretion of saliva. The motions, although not very frequent, were never solid, and became more and more offensive; very offensive flatus was also passed. Vomiting occurred only once, as the result of cough in the morning. There was never any slime or blood with the motions.

There was no improvement under careful dieting and with the administration of intestinal antiseptics.

Eight weeks after the illness commenced the most marked symptoms were—some amount of pallor with cachexia, great emaciation, and flabby muscles. There were no signs of organic disease in any part of the body. There was no growth in the rectum, the mucous membrane of which was somewhat boggy to the touch. The diagnosis made on the first examination was that of intestinal intoxication, the cause of which was not obvious.

The patient was placed in a private hospital, in order to carry out more complete observation. It was found that the body temperature was irregular. During the first week there was no febrile rise, but an occasional subnormal fall. During the second week, on three days there was a rise of temperature to 99·8°, 100°, and 100·8°, while in the third week there was a similar, although not so great, tendency to rise above normal.

The intestinal evacuations were not very numerous—from one to three daily, but were always liquid, and extremely offensive. Two very large motions were washed with water, and found to contain no blood or slime. Several largish lumps which were discovered proved to be pieces of apricot, which, on close inquiry, were found to have been eaten at the commencement of the illness, eight weeks previously.

Repeated examination failed to discover any physical signs indicating the cause of the intestinal decomposition. The treatment adopted at this stage was flushing the colon with solutions of boric acid, but these had to be stopped on account of the great prostration produced.

The wasting continued, the patient losing 11 lbs. in fifteen days, so that his condition had rapidly become desperate. He was now lying in bed, extremely weak, greatly emaciated, with a dry tongue, complete loss of appetite, but with his mental faculties intact. The deep inguinal glands of the right side were enlarged.

At one examination of the abdomen a mass was felt in the right loin, which, it was considered, might possibly be a new growth in the ascending colon, and at a consultation with Mr. R. J. Godlee it was decided to explore the abdomen, in order to detect the cause of the disease. At the operation it was found that the mass felt in the right loin was the kidney, which had become readily palpable, owing to the great emaciation. On tracing the colon down towards the cæcum it appeared thickened, and an examination of the appendix showed that it was enlarged, being both elongated and thickened, while there were some calcareous glands between the ileum and the cæcum. The appendix being obviously diseased, it was decided to remove it, and two calcareous glands and one other enlarged gland were removed.

An examination of the appendix showed enormous thickening of the coats, with the exception of the peritoneal coat, except for half an inch at the junction with the cæcum; at this point the coats were normal in thickness. The contents of the appendix were extremely fœtid, like the motions, and consisted of one or two fæcal concretions, as well as much liquid matter. Two small erosions were seen in the mucous membrane, near the lower end. A microscopical examination showed chronic inflammation of the mucous membrane and the muscular coat. No bacteria were discovered in the tissue. The non-calcareous lymphatic gland removed also

showed no bacteria. In a few areas the cells were somewhat degenerated, but there was no definite necrosis.

The diseased appendix was considered as the *fons et origo mali*, and this proved ultimately to be the case.

After the operation the patient was in an extremely weakened condition, and showed occasional slight rises of temperature, due to suppuration round the stitches of the wound. There was, however, no deep suppuration. The anorexia still continued, as well as the passage of the fœtid motions. The enlarged inguinal glands returned to their normal size shortly after the operation. Great difficulty was experienced in feeding the patient, although there was no vomiting. Recovery, however, although it was gradual, ultimately became certain.

The patient went to the country, and in June, 1900, six months after the operation, a small quantity of albumen was discovered in the urine, with some casts. At the end of July, 1900, the bowels were only occasionally loose, and possessed no fœtor. There was branny desquamation of the skin. The patient was gaining weight, and this continued to be the case until ten months after the operation, when the usual weight was attained.

During this time the chief interest centred in the condition of the urine. Six months after the operation I examined the urine myself and found a trace of albumen, with a few granular casts and no pus, the specific gravity being 1017. One month later there was still a slight trace of albumen in each of two specimens; but three weeks later there was no albumen in the night urine, and the merest trace in that of the morning. Four subsequent examinations of the urine within the next two and a half months showed absence of albumen.

The patient was now, ten months after the operation and twelve months after the onset of illness, completely restored to health, and without a sign of disease.

Disease of the appendix, causing acute or subacute disease, is usually associated with definite physical signs

on the right side of the abdomen, in the iliac or lumbar region. The case here recorded is of interest, inasmuch as there was severe illness, due to chronic disease of the appendix, in which the main symptom was the decomposition of the intestinal contents, causing a profound intoxication. In adults prolonged intestinal decomposition is usually associated with obstruction in one or other part of the colon; and in this case, considering the age of the patient, this was regarded before the operation as the most likely cause. Chronic dysentery may also be associated with prolonged intestinal decomposition, but a dysenteric affection did not enter into the history of this case.

Besides the main fact that chronic appendicitis was the source of the intestinal decomposition, one or two interesting points may be drawn attention to. One is the long retention (two months) in the intestinal tract of comparatively large pieces of apricot, in a case in which there was continuous looseness of the bowels. This retention of indigestible solid masses is observed in cases of obstruction of the colon and of the pylorus, in the latter case even when there is vomiting.

The second interesting point is the condition of the lymphatic glands. The superficial lymphatic glands in the inguinal region and other parts were easily felt. This may have been due to the great emaciation of the patient; but on the right side, near Poupart's ligament, one deep inguinal gland more particularly was distinctly enlarged, and one of the glands removed at the operation from the abdomen was also enlarged. The enlargement of the glands rapidly disappeared after the operation.

There was in this case no bacterial infection as far as could be discovered; the wells of the thickened appendix showed no bacteria, and there were none in the microscopic sections of the lymphatic gland. The enlargement of the glands is probably to be considered as part of the intoxication process.

DISCUSSION.

Mr. RICKMAN J. GODLEE.—The interesting thing from a surgical point of view is the fact that the appendix was so large, as large as one's thumb, and yet it could not be felt. The pain, again, was described as near the umbilicus, yet the appendix lay to the outer side of the cæcum. The glands taken away from the little angular space between the end of the ileum and the cæcum were calcareous, and this it was thought might have been due to old tuberculous disease. I was struck with the large size of the gland in the inguinal region, and with the fact that the enlargement disappeared after the operation. I was aware that there are intimate connections between the inguinal glands and the space I have alluded to, but it was new to me to find that one could get enlarged glands there as the result of appendicitis.

Mr. CHARTERS SYMONDS.—I wish to raise the question whether the interpretation which the author has given is the correct one. The appendix is described as very large, and as having a very free communication with the cæcum, and it is a question whether such an appendix could give rise to the septic disturbance to which this malady was attributed. Would it not be more correct to say that the patient was suffering from colitis—ulcerative colitis—and that the appendix participated in this general malady? In that sense we should have to look at the operation as not having contributed to the patient's recovery, but that recovery took place spontaneously, as these cases do recover. There is the looseness of the bowels, the foul odour of the motions, the irregular temperature, and profound emaciation, all conditions which are known to accompany ulcerative colitis. In the cases that recover we cannot tell whether they were due to primary appendicitis in the absence of an operation. I am reminded of a case of a patient who had five attacks; in all there was a temperature more or less hectic in type, and irregular, looseness of bowels, and foul odour of the motions, with profound emaciation. As the patient has recovered the case remains obscure. I should hesitate to conclude that any condition of the appendix could give rise to such a malady as that which the author has described. Another question is whether the appendix may not give rise to obscure septic conditions in a more acute form. I can best explain my meaning by relating a case, that of a gentleman who was taken suddenly ill with pain in the belly, after twenty-four hours' malaise, without any localising symptom. When I saw him in the third week of his illness there was a high temperature, one furious rigor and two milder ones, and moderate emaciation. As he did

not improve, and the general symptoms were alarming, suppuration of the gall-bladder was thought of, but the evidence did not appear to me conclusive. Nevertheless I exposed the gall-bladder, and found it healthy, but I took advantage of the opportunity to explore the appendix, which proved to be adherent. This I removed through a separate incision, closing the upper wound, and he got well. The appendix was diseased and perforated, and there was a small cavity with some grumous material round its end. He did not get well immediately, for he developed phlebitis, but except for some œdema of the leg he is now well. I have seen several cases characterised by high temperature, rigors, and prolonged illness, with nothing to explain them; some have got well and some have died. It was rather in this connection that I was interested in this subject of the appendix, but I repeat that I doubt whether an appendix which has a free communication with the cæcum, as the author's patient had, could give rise to the series of symptoms which he has described. I would submit for discussion that it might be looked upon as a case of colitis. As to the seat of the pain, I have noticed this before in a genuine appendix case, which was peculiar in that there was a calcareous concretion lying outside the appendix, and the patient was relieved by its removal. This struck me at the time as being very peculiar.

Mr. J. H. Morgan.—Apart from the special interest of this case I have a personal interest therein in that the patient was a very old friend of mine. I had known him for thirty years at a time when he was addicted to athletic performances; he had won several three-mile races, and to do this he must have been a man of much physical stamina. Such a subject could hardly have suffered from tuberculous disease in his youth, or if so it is very consoling to those who have to treat similar conditions. I may point out that in the paper he is described as having suffered from looseness of the bowels on his return from Norway, but he came to stay with me on his return and diligently fished in the worst possible weather, and I can certify that there was no looseness of the bowels while he was staying with me. I know that he returned home in robust health, and it was not until a month later that his attack began, on November 7th. What I want to learn is to what this condition of the glands is attributable. Was it to tuberculous disease, or can it have been that at some period of his infancy he had suffered from appendicitis which had produced a condition which ultimately determined the state of things discovered at the operation, viz. some slight constriction of the appendix at its junction with the cæcum which had become more marked as time went on and so allowed this distension of the distal portion of the appendix and the accumulation of decomposing matter? I think the presence of this decomposing matter accounts for

the toxæmic condition of the system. This would account for the condition of the glands even though no bacteria were found therein. The clinical features of the case are as interesting as they are unusual, and the case adds another difficulty to appendix cases which, I think, are still far from being understood.

Dr. HALE.—The contents of the sac were so foul that they had to be removed from the room within a minute or two of their being taken away.

Dr. MARTIN.—I think Mr. Symonds has gone rather out of the way for an explanation of the case. If he had seen the patient before and after the operation. I think he would have concluded that the appendix was the cause and not the result of the malady. There was not simply a free communication with the cæcum, but a sort of neck, and inside the cavity was filled with foul matter having the same odour as the motions. This must have been due to the predominance of a particular variety of bacterium, and this predominance could only take place in a tube. The case was certainly unlike any case of ulcerative colitis I have ever seen. The motions contained no trace of blood or mucus, and were altogether unlike those of colitis. Moreover, the patient improved almost immediately. Supposing, however, that there had been ulcerative colitis or other infection of the colon, and that the appendix had participated in the disease, one would not have expected to find the appendix joined to the cæcum by a normal portion. The only explanation of the case appears to me to be that the appendix in some way formed a sort of test-tube, its decomposing contents escaping into the intestine and producing intestinal decomposition. I have seen one other case which suggested to me that a diseased appendix might produce intestinal decomposition, but in that case no operation was performed, so that the case remains in doubt. I agree with what Mr. Morgan has said as to the gland enlargement being due to a toxæmia; it was a true intoxication. I remember a case after parturition without septic infection in which there was enlargement of all the superficial glands.

A CASE OF PERNICIOUS ANÆMIA

WITH OBSERVATIONS REGARDING

MODE OF ONSET, CLINICAL FEATURES, INFECTIVE NATURE, PROGNOSIS, AND ANTISEPTIC AND SERUM TREATMENT OF THE DISEASE

BY

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Notes of Case.

Case 1 (*Charing Cross Hospital*).—Name of patient, A. L—, aged 37; occupation, traveller; admission, July 4th, 1900.

Complaint on admission.—"Great weakness, breathlessness, and palpitation."

Duration.—About two years.

Family history.—Father died at thirty-seven from the effects of a *stroke of lightning*. Mother alive and well, sixty-three years old. Two brothers alive and well. Three sisters also alive and well. One sister died of cancer of breast at thirty-six years of age. Nothing else of importance in family history.

Past personal history.—(*a*) Twenty years ago the patient, while killing pigs condemned for swine fever, was inoculated by a wound in the finger. He was very ill for a few days, with high temperature, urticaria-like rash on the body surface,

great swelling, etc., but eventually recovered completely. (*b*) He had typhoid fever while a child. Recovery complete. (*c*) Four years ago he suffered from three accidents, all within a short space of time, viz.:—(1) Head injury caused by falling out of a trap; (2) kick from a horse over the left eye; (3) kick from a horse over the spleen. He seems to have recovered almost completely from all these injuries, the only indications nowadays being occasional sensations of numbness in the regions of the first two injuries, and a certain tendency or liability to headaches upon slight provocation, such as an unusual amount of brain-work (calculations, etc.), excitement, or irritation; and, again, he is liable to giddiness on stooping down for any length of time. (*d*) He has also suffered from influenza twice, the first occasion being three years ago, when his principal symptoms were "head;" and again six months ago, when they were again most prominent, and after which his present condition became much more aggravated.

Habits and general surroundings always seem to have been excellent. He describes himself as being a very "careful living man," particular about his food, health, and general comforts. He always appears to have been in a position to gratify these desires. He has passed through several grades of occupation:—(1) He began life on his father's farm in Bedfordshire; then became (2) butcher at Kilburn for three years; (3) charge of stables at Bon Marché for twelve years; (4) bought a public laundry for himself at Willesden, and kept this going well until April of this year, when he gave it up, owing to the great decline in his general health and consequent inability, through weakness, to give that care and attention to his business which was essential for its success. Latterly he has had a very easy and profitable occupation as a traveller for a brewery in Kilburn, which gives him very little anxiety and exertion; but even this he has recently been compelled to give up.

Present illness began two years ago, when the patient noticed his appetite was poor, weight coming down; colour, which had always been red, disappearing and becoming yellowish at times, and what was most prominent of all, an almost constant pain in the stomach and side (over spleen), and periodically acute attacks of *severe pains in the mouth and stomach.* On investigation still further into these curious periodical attacks of pain which he complained of, it was ascertained that at this time

(two years ago) he was greatly troubled by what he describes as a *sore mouth*. It began by pain and swelling of the gums, then the teeth became sharp-edged in feeling, so that they tasted like "china" in his mouth, and seemed as if they would at any moment cut his tongue to pieces. In twenty-four hours after this the tongue itself would become almost unbearably sore, and on inspection patient noticed big red patches on the dorsum and edges. In endeavouring to describe the sensation of this sore mouth, he said:—"The tongue felt as if it had no covering, as if it was quite raw, so that when I put a piece of bread in my mouth at meals it felt like sandpaper." It never seems to have bled; and it is interesting to notice that when the attack, which usually lasted two or three days, was over the patient could eat beef-steak or any other food. During the attack his food consisted of milk and bread sop. The attacks came on about every three weeks, and were followed and accompanied by gastric symptoms, which will be referred to later.

This state of matters continued until about Christmas, 1899, when patient had three very bad teeth extracted; and he is certain that from that date the mouth condition diminished very considerably in severity. He has had mild complaints since; but *the* complaint which has been most prominent since that time has been the *gastric pains*. He has constantly suffered during the last twelve to eighteen months from a gripping, vice-like pain in the region of the epigastrium, always more marked at times, *e. g.* after a mouth attack, when he had worked hard and exhausted himself, or when annoyed or irritated by anything. His appetite was very variable, depending to a great extent upon the condition of his mouth, but always improved after the mouth trouble was over for a time (interval between two attacks). He has had recently a tendency to *nausea*, which became aggravated in its severity when anything unpleasant or distasteful to sight, smell, or taste was present. He was never actually sick, except after taking some medicine which he had had during an intermittent illness (influenza). Nausea and *retching* were often present, and the latter was particularly severe if the stomach was empty.

During the last twelve months the patient has felt himself grow perceptibly weaker, and incapable of hard work.

Breathlessness, palpitation, and giddiness have gradually forced

themselves upon him; and now he can distinctly recollect how he has noticed the gradual onset of the *lemon yellow colour* of skin all over the body, but states that it has constantly varied in intensity. The most marked features of late have been the great *weakness*, together with the nausea, etc., referred to above; and in addition, *pains shooting down the limbs, numbness, tingling in the shins*, acute pains in the clavicular regions at times which almost arrested breathing. The patient has been treated all along for chronic catarrh of the stomach, and his mouth has been relieved by borax, glycerine, and chlorate of potash lozenges. His diet was never the subject of special comment; he generally took what he thought would suit him. He came to Charing Cross Hospital on June 29th for examination, and after hearing the history and examining the blood, the case was diagnosed as "Pernicious Anæmia," and was recommended to come in as soon as possible for treatment.

Condition on admission (July 4th, 1900).—Height, 5 feet 6 inches; weight, 9 stones 7 lbs. Appearance:—fairly well nourished; very anæmic; slight lemon colour.

Alimentary system.—History: oral, gastric, and intestinal—as above described.

Teeth.—Two incisors, lower jaw, exposed and carious at their necks; gums receding, inflamed. Necks covered with tartar. They have been in this condition for ten years, and have bothered him.

Upper jaw: right side.—Bicuspids and two molars absent, Wisdom tooth remains; shows carious cavity, and gum around slightly swollen and inflamed. *Left side.*—Canine represented by a necrotic root. *Lower jaw.*—Back tooth, left side, represented by a rotten root. Other teeth sound. *Tongue* normal, gums somewhat anæmic; otherwise normal. The *stomach* slightly enlarged; complains of localised severe pains over the epigastrium. Patient cannot bear the least pressure here. The *liver* quite normal. *Spleen* slightly enlarged. *Bowels* somewhat loose, and fæces paler than normal.

(2) *Circulatory system.—Heart* slightly enlarged in its transverse diameter. Over pulmonary and mitral areas systolic murmurs, soft and low in character.

(3) *Respiratory system*, with the exception of the breathlessness, normal.

(4) *Nervous system.*—Complains of tingling and numbness, shooting pains, etc., as described above.

(5) *Urinary system.*—Urine dark sherry in colour; urobilin; no albumen, or bile, or sugar.

(6) *The conditions observed in the blood.*—The red blood-corpuscles were markedly altered in size and shape, showing poikilocytosis; numerous nucleated R.B.C. were present. Hæmoglobin 35 per cent., and R.B.C. 1,500,000 per c.mm. (30 per cent.).

Progress of Case.

Period 1 (July 4th to 9th).—*Treatment.*—Patient was put upon milk diet; an antiseptic mouth wash; liq. hydrarg. perchlorid., ♏xxx, thrice daily as an intestinal antiseptic; with carbonate of ammonium (gr. 3), and tincture of digitalis ♏v as a stimulant.

July 6th.—Patient had an attack of sickness yesterday, preceded by much pain in the usual situation, at 4 p.m., about quarter hour after taking medicine (vomit bilious in character, according to patient), after which he was all right and had a good night's rest. This morning he feels very sore in the stomach, and legs ache very much from knee to ground. The tongue has a prickly feeling, which makes it feel "as if it were clinging to roof of mouth." On examination, nothing is made out except a *small red patch in the middle line*, almost at position of hard and soft palate; patient puts his fingers on it and says it is "*raw.*"

Blood.—Examination on July 6th. Great difficulty was experienced this morning in getting away blood at all for examination. On puncturing the fingers scarcely a drop came away; and it was only on pressure to the part, and allowing hand to hang before puncture, that any was forthcoming.

7th.—Blood examination this morning showed red corpuscles 1,350,000 (27 per cent.), with distinct poikilocytosis, and many nucleated reds were seen. Pain in the side (spleen) and stomach, continue as before. Feet very cold; mouth distinctly better; no sign of irritation.

8th.—Better this morning; pain in stomach and side easier, but still present in limbs; mouth quite easy; wash has improved it.

9th.—Patient feels unwell this morning; complains of pain

in limbs (usual situation), stomach, and heart—described as a "feeling of wind with pains like pressure;" the mouth is causing some trouble by pains around the first premolar on left side; the local signs of condition are *nil*. The stomach is dilated slightly. Temperature 99·4°.

Urine high-coloured.

Temperature.—(See Chart.[1]) *Blood.*—Corpuscles 27 per cent.

Period 2 (July 10th to August 16th = five weeks).—*Treatment* as above, *plus* four injections of antistreptococcic serum.

10th.—*First injection* of antistreptococcic serum made, 10 c.c., at 6 p.m. last night.

Patient feels tired and worn out this morning; has passed a sleepless night. Temperature 99°. Pains are complained of all over body, particularly over right side, and stomach and legs. He looks flushed. Pulse 98. Mouth "dry"—nothing obvious on examination.

11th.—Patient feels distinctly unwell to-day. Temperature 101·6°; complains of pains in right side of stomach (hot burning), and slightly on left side. Pulse 120. Headache severe.

12th.—Temperature 102·6°; pulse 120. Although temperature and pulse are still high, the patient does not feel anything like as unwell to-day as yesterday. The principal complaint is headache, felt principally at vertex; pains in stomach and side as before; complains also of flatulence and retching, although food is still peptonized; mouth is very dry (lemon drink given); great thirst. Legs remain the same, and arms also ache badly. Throbbing pains, lightning like. Blood examination, corpuscles 1,580,000 (31 per cent.). Hæmoglobin 35 per cent.

13th.—Temperature 99°; pulse 100. Patient feels more himself to-day. Headache has passed to occiput, and is not so severe. The pain in stomach, side, and limbs is better. Motions are liquid. Mouth better.

Blood.—Corpuscles 31 per cent. Hæmoglobin 35 per cent. Second injection of serum at 8 p.m.

14th.—Rigor for quarter hour at 1 a.m; sleepless and restless night. Feels better this morning—very little pain complained of. The rigor started in left shoulder, and passed down whole left side. Right side unaffected.

[1] For chart of this case see author's 'Pernicious Anæmia,' Charles Griffin and Co., 1901.

15th.—Temp. 100·2°. Complains of severe pains in head. Otherwise as before; slept well; appetite good.

16th.—Temp. 100·8°; pulse 96. Blood 1,800,000 (36 per cent.). Hæmoglobin not estimated. Great difficulty experienced in getting blood for ordinary numerical estimation. Pains and discomfort are complained of. Motions are more solid; liq. hydrarg. perchlor. is reduced.

17th.—Temp. 99·2°; pulse 88. Headache not so violent, but with sharp pains; soreness on left side from point of last injection down left groin and leg. Mouth and tongue not sore today. Patient has difficulty of passing water lying on his back.

20th.—Patient feels much better. His head feels better, but complains of sweating on his head. Soreness in side is better, and no difficulty in passing water. Temp. (10 a.m.) 98·4°; pulse 76. Corpuscles 2,530,000 (50 per cent.).

21st.—Patient describes himself as better altogether.

22nd.—Third injection (5 c.c.).

23rd.—*Blood-count*, 2,635,000 (52 per cent.). Blood flowing much more easily than formerly. The corpuscles were noticed to be more even in shape, approaching more nearly the normal cells. Hæmoglobin obviously more abundant, but not estimated. Patient describes himself as improving. Sleeps well. Temperature normal.

25th.—Patient improving daily. Temperature steady (see Chart). Yesterday food changed; more solid nature; fish, etc. Patient relishes the change. All aches, pains, etc., have disappeared of late.

31st.—Patient has not felt so well since Saturday, 28th. Complains of pains in head, feeling of thickness or dulness. Stiffness in shoulders and neck, soreness under ribs. Some palpitation on movement. Skin all over body is clearer. There is a certain amount of rawness in the perineal region—an old complaint which patient suffers from periodically. *Blood-count* 2,845,000 (56 per cent.).

August 1st.—Blood:—(W.H.) R.B.C. 3,290,000 (65 per cent.), W.B.C. 17,000. Hæmoglobin 75 per cent. Patient greatly improved in looks.

2nd, 11 a.m.—Last night, fourth injection (5 c.c.). Afterwards no sleep until 4 a.m., when he had an hour's sleep. (Trional grs. xx given, before grs. x with no effect)—slept

again this morning—appetite fairly good—complains chiefly of pain in the left side, near seat of injection and passing into flank; looks flushed. Temperature practically normal (98·6°). Pulse 120. Headache improved.

3.30 p.m.—Patient feels much better this afternoon.

3rd.—Temp. 99° this morning; slight reaction has set in after the injection on the 1st. Pulse 120. Patient feels better to-day.

4th.—Pulse 120. Temperature last night rose to 99·8°. Now 99°; slept well. Troubled with headache. Complains of flatulence after food. Locally, still some brawny œdema, left flank, close to site of injection. *Urine.*—High colour, heavy deposit of red urates.

7th.—Feeling better; up each day from 12 to 6 p.m. Looking well. Pulse 84. *Urine normal in colour. Much lighter than any time since admission.* Blood 2,750,000 (55 per cent.). Hæmoglobin 70 per cent. Slight looseness of bowels to-day (twice).

8th.—Two lower incisors, formerly described, edges red and inflamed, and *covered with pus*, despite the fact that he has used an antiseptic mouth wash daily for a month. Swabbed out with 1 to 20 carbolic acid. Edges bleed freely. Tartar removed. Gums to be swabbed daily with 1 to 20. Slight desquamation of skin over face. No local tenderness over abdomen. Pulse 78. Temp. 97·8°. *Urine.*—Straw colour. Sp. gr. 1018. No albumen.

10th.—Blood examined. Corpuscles 3,360,000 (67 per cent.). Hæmoglobin 72 per cent. Corpuscles normal in appearance. *Feeling very well.*

15th.—Three teeth drawn. Back wisdom upper jaw; lower jaw left wisdom; upper canine. *Lower incisors.*—Gums previously receding, now grown up around tooth and looking healthy. They have not been right, he says, for ten years.

16th.—Patient goes out to-day. Pulse 84. Appetite good. Temp. 99°. Urine darker, 1025. No albumen. No indican.

Results of Five Weeks' Treatment.

Urine.—Very pale: urates appeared in urine on the first and second days succeeding injections.

(6) *Blood.*—	R.B.C.	Hæmoglobin.
July 4th	1,500,000 (30 per cent.)	35 per cent.
„ 7th	1,350,000 (27 „	
1st inject.:		
„ 9th		
„ 12th	1,580,000 (31 „)	35 „
2nd inject.:		
„ 13th		
„ 16th	1,800,000 (36 „)	
„ 20th	2,530,000 (50 „)	
3rd inject.:		
„ 23rd	2,635,000 (52 „)	50 „
„ 31st	2,845,000 (56 „)	
4th inject.:		
Aug. 1st	3,290,000 (64 „)	75 „
	W.B.C. 17,000 per cmm.	
„ 7th	2,750,000 (55 per cent.)	70 „
„ 10th	3,360,000 (67 „)	72 „
	R.B.C. normal; no poikilocytosis.	

Total result in blood.—An increase of 40 per cent. of red corpuscles and 37 per cent. of hæmoglobin.

Period 3 (August 16th—September 26th = six weeks).—Sent to the country. *Treatment.*—Oral and intestinal antisepsis as before. Light ordinary food, chiefly milk. ʒj of Syrup of Hypophosphites three times daily as a tonic. Arsenic still withheld.

September 26th, 1900.—Returned. Looking stout. He has put on 7 lbs. in weight. Weight is now 10 stone. Good colour. Complains still of numbness and dead feeling of finger-ends. Mouth and teeth very clean. Digestion normal.

Blood.—Red corpuscles 3,200,000 (64 per cent.). Hæmoglobin 80 per cent.

Result.—The improvement in weight, colour, and appearance is greater than the improvement in blood. The latter only shows an increase of 8 per cent. in hæmoglobin.

Period 4 (September 27th—November 8th = six weeks):—*Treatment.*—Oral and intestinal antisepsis as before. *Medicine.*—Liquor Arsenicalis ♏iiss ter die.

October 4th, 1900.—Looking still better, and feeling very well. Weight 10 stone 2 lbs. Appetite good; stomach com-

fortable. Bowels regular, generally once, and sometimes thrice daily. Urine pale straw-colour. He notes himself "it is much better;" that sometimes it is very dark, *e. g.* last week; and that it is always darker when he is not feeling very well.

His tongue looks red. He states it has been very sore last four days. "Feels cracked all over" when he takes anything to eat or drink. Last attack of the kind was four weeks ago, lasting about a week.

His chief trouble now is that his fingers feel perfectly numb, so much so that he cannot button his clothes, owing to want of feeling in fingers. This affects both hands, and extends up to elbows. Calves of legs feel weak, but there is no numbness in them.

November 8th, 1900.—Improvement still continues. Looks ruddy and stout. Weight 11 stone 2 lbs. (an increase of a stone in one month.

Blood.—Red corpuscles 4,040,000 (80 per cent.). Hæmoglobin 90 per cent. = increase of 16 per cent. in corpuscles, and 10 per cent. in hæmoglobin.

Period 5.—Further progress (November 8th—January 17th, 1901 = 10 weeks). *Treatment* as before. Arsenic increased to ♏v till December 21st, then reduced to ♏iis.

December 21st, 1900.—Looking very well. Weight 11 stone 2½ lbs.

Blood.—Red corpuscles 4,500,000 (90 per cent.). Hæmoglobin 92 per cent.

January 17th, 1901.—Looks in robust health.

Blood.—Red corpuscles 4,550,000 (91 per cent.). Hæmoglobin 104 per cent.

Tongue clean. Digestion good. Urine pale. Only symptom remaining is slight numbness in the tips of his fingers.

Remarks.

The case is of interest in connection with the result under the special line of treatment employed. But it is of additional interest—and for that reason is now brought before this Society—inasmuch as it presents in itself every clinical feature which I consider characteristic of this disease, as regards—

(1) Its antecedent history.
(2) Mode of onset.
(3) Character of its blood-changes.
(4) Character and grouping of its symptoms.
(5) Diagnostic features.
(6) Infective nature of the disease, and its relation to oral and gastric sepsis.
(7) Its response to a special line of treatment, based upon my observations regarding the infective origin and seat of infection of the disease.

Conclusions regarding the Nature of the Disease.

The following are the conclusions I have arrived at as the result of fifteen years' investigations—histological, experimental, chemical, clinical, and ætiological—regarding the nature of this disease.

1. Pernicious anæmia is a chronic infective disease of septic origin.

2. It is the result of a special infection of the mucosa of the digestive tract, especially of the stomach; frequently also of the tongue, and of the intestine.

3. The effects are chronic infective lesions of the tongue and stomach or intestine, which can be seen (in the tongue) to heal up in one part only to spread to another, causing in time deeper-seated changes, *e. g.* ulcers of the mouth and tongue, chronic glossitis and atrophic changes in the tongue; gastritis with atrophy of gastric glands; and localised enteritis.

4. In this infection, oral sepsis arising in connection with long-continued and neglected cario-necrotic conditions of teeth plays an essentially important antecedent and concurrent part by creating the local conditions of the mucosa ("septic" stomatitis, gastritis, and enteritis), which permit the infection to take root.

5. In the vomit the septic nature of the catarrh of stomach can be demonstrated in every case.

6. One element in the infection (in pernicious anæmia) is streptococcal; but this is not the only one. It

probably derives its special (hæmolytic) properties from being of a "mixed" character.

7. For the infection to occur it is essential that the mouth, stomach, or intestine be already from some cause the seat of disease; the most potent antecedent cause is "oral sepsis," and "septic gastritis" arising in connection with oral sepsis.

8. The gastric and intestinal symptoms—sickness, retching, vomiting, looseness of bowels, and diarrhœa—so often noticed (and I find even more common than is stated, being recorded in over 80 per cent. of cases) are the local manifestations of the infection; while the excessive destruction of blood taking place in the portal area is the result of the action of its poisons absorbed into the blood.

9. The fever so commonly met with is not an accidental occurrence—the effect of weakness,—but is a feature of the disease, a result of the infective process itself; and its variations correspond to variations in the activity of that process.

10. Such variations are common—from week to week, sometimes from day to day—in the progress of the disease, even when it is running a fairly progressive course.

11. In addition, however, the course of the disease towards the fatal termination is often marked by one—sometimes by two—periods of marked improvement, lasting, it may be, many months, or a year or more, followed by relapses. This character of the disease I have come to regard as the result of a relative immunity, unfortunately only temporary in its nature, conferred by the disease itself—an immunity accelerated and greatly strengthened for a time by suitable medicinal treatment, notably by administration of arsenic.

12. The tendency to relapse may, however, be due to the fact that, hitherto, the immediate sources of infection, viz. the oral sepsis, not having been removed, the patient has always been left exposed to reinfection.

Gastro-intestinal Site and Infective Nature of the Disease.

On this point, the most important of all in connection with the disease, the conclusions I have formed are, as already mentioned, of a very definite character.

The disease, I conclude, is not only a special form of anæmia, but a most definite infective disease, localised to the mucosa of the alimentary canal, causing a most definite and characteristic group of effects, both clinical and pathological, which enable it to be distinguished during life and after death.

In this infection sepsis, both oral and gastric, plays an important antecedent and concurrent part.

These conclusions are of such a character, that if taken by themselves, without regard to the continuous line of investigations on which they are based, one might perhaps doubt whether they could possibly refer to the disease originally described by Addison as "idiopathic, —occurring without any discoverable cause whatever;" and subsequently defined by Dr. Pye-Smith (1883), on the strength of the facts supplied by thirty years' additional observations, "primary, autochthonous—without any symptoms, and without any lesions that cannot be explained as directly due to the anæmia."

And yet it is to this anæmia that the conclusions refer. Moreover, it is to this alone—the so-called "primary" "cryptogenetic" form of the disease. The "secondary" forms described by Biermer, Eichhorst, Ehrlich, are in my experience totally distinct conditions.

I recognise no "primary" or "secondary" forms of the disease, any more than I recognise primary and secondary forms of typhoid fever or tuberculosis. As with other infective diseases so with this one ("Addison's anæmia") there is no reason why it may not occasionally occur in patients already the subjects of other diseases; but even when it does, it can be recognised by its definite

clinical features as clearly as if it occurred alone, just as typhoid fever can be recognised, although occurring in a patient the subject of tuberculous disease.

In the accompanying scheme I have represented graphically the course and results of the investigations —histological, experimental, chemical, clinical, and ætiological—extending over fifteen years, on which the above conclusions have been based.

Full details are given in my work 'Pernicious Anæmia,' C. Griffin and Co., 1901.

In no case have the conclusions been lightly formed; and they differ from most other conclusions regarding the ætiology of the disease in this respect—that while most others are based on clinical grounds only, the basis of these is essentially pathological. It is the series of investigations regarding—

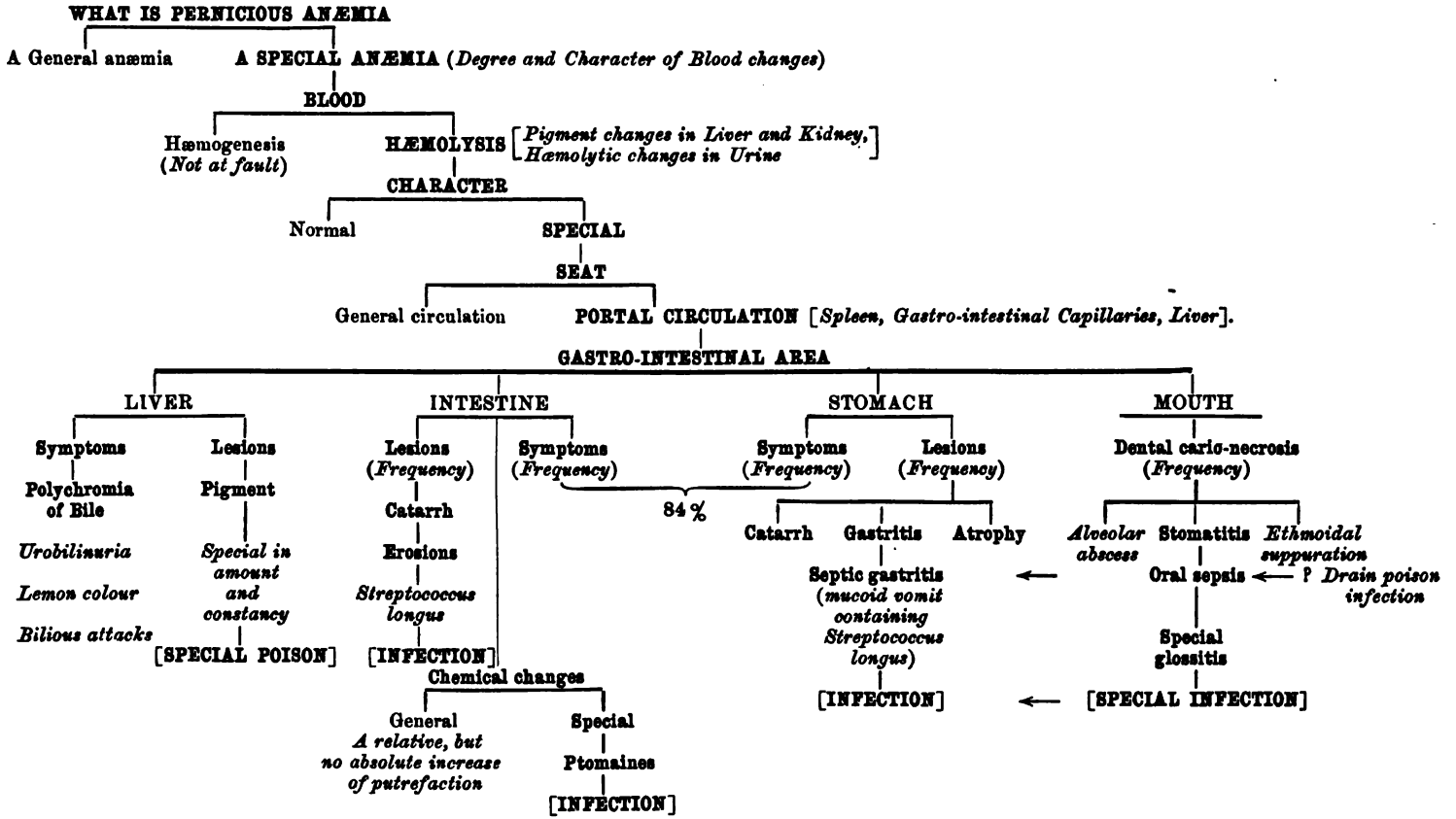
(1) The Hæmolytic Nature of the disease;
(2) The Special Character of the hæmolysis;
(3) The Portal Circulation as its seat;

that constitute the basis of my conclusion regarding the special nature and gastro-intestinal site of the disease processes underlying the hæmolysis of this disease.

And all my later observations and conclusions and studies regarding the frequency, character, and possible significance of the symptoms and lesions connected with this tract, derive their importance in my eyes chiefly, if not solely, from the circumstance that they are in entire agreement with these pathological conclusions (see Scheme).

Without the basis here indicated, it would not be justifiable, for example, to attach to the whole group of oral, gastric, and intestinal symptoms, and to the special lesions met with in the tongue, the significance I now do, as denoting the existence of a special infection in this tract.

SCHEMATIC REPRESENTATION OF COURSE AND RESULTS OF AUTHOR'S PATHOLOGICAL INVESTIGATIONS REGARDING THE HÆMOLYTIC NATURE, GASTRO-INTESTINAL SITE, AND INFECTIVE ORIGIN OF PERNICIOUS ANÆMIA.



Definition of the Disease.

Hitherto the feature of the disease to arrest chief attention has naturally been the *anæmia*—the progressive blood change,—and all other symptoms have been studied in relation to this. The disease has been regarded as an anæmia complicated from time to time by other disturbances—digestive, nervous, circulatory, etc. The result has been to obscure some of the chief characters of the disease, and certainly to hide much of their proper relation to each other. The conclusion I have come to is, that it is an *infective disease characterised by anæmia* with *definite local and general* effects—not merely an anæmia occasionally complicated with such effects.

The definition which I have formulated for the disease is the following:

Pernicious anæmia is a chronic infective disease localised to the alimentary tract, *caused by* a definite infection of certain parts of the mucosa of the alimentary tract either of the stomach, tongue or the intestine. In this infection, sepsis, both oral and gastric, plays an essentially important antecedent and concurrent part. It is *characterised by*—

(1) Intermittent destruction of blood and increasing anæmia (and all the other pathological and clinical changes consecutive to these—*e. g.* anæmia, lemon colour, urobilinuria, hæmorrhages, dyspnœa, palpitation, œdema), as the result of the absorption and hæmolytic action of poisons into the blood.

(2) Periodic disturbance of the alimentary tract—tongue, stomach, or the intestine—as local effects of the infection in the alimentary canal; and

(3) Occasional "toxæmic" attacks, characterised by fever, sweatings, general nervous symptoms; not infrequently by effects—*e. g.* numbness, tingling, ataxia, absence of reflexes—denoting deeper nervous changes, such as peripheral neuritis, sclerosis of the cord.

The foregoing characters of the disease are well represented in the case described, and I shall comment on them in the order mentioned.

Antecedent History.

The patient was a "careful living man," who had always enjoyed good health, and had been well fed and nourished.

Such a history is, in my experience, one of the striking peculiarities of the disease, namely, it occurs, as Addison described, "without apparently any discoverable cause."

In my experience, it is met with in the well-to-do as much as in the poor, in the well-fed as much as in the poorly nourished, in the athletic man as much as in the weakly, in the man who has spent his whole life in the country as much as in those living in towns, in those whose health has previously been good (as in the present case) no less than in those already debilitated by disease.

It is this class of facts that has satisfied me that in the production of this form of anæmia general conditions of life are not those at fault; that its origin is to be sought elsewhere—in some special conditions, rare, fortunately, in incidence, but common to all classes, irrespective of station, mode of life, character of food, of nutrition, or general surroundings.

That special condition my observations show to be a special infection, localised to portions of the mucosa of the alimentary tract, having its chief seats in the tongue and in the stomach, an infection in which long-standing sepsis, oral and gastric, plays an essentially important antecedent and concurrent part.

In his original description of the disease—that the disease occurred in the absence of the ordinary factors causing anæmia—Addison, then, in my judgment laid,

the ætiological foundation of our knowledge of this disease broad and deep.

The different conclusion come to by Biermer, so largely accepted by nearly all later observers—namely, that all ordinary causes of anæmia are potential causes of this disease, if only they are severe enough—has, in my experience of the disease, no real basis. The disease cannot, in my experience, be produced by ordinary anæmia-producing factors, however severe; and cases of this kind can be successfully excluded, both during life and after death, by the absence of the characteristic groups of symptoms, and of the no less characteristic pigment changes I have described.

Mode of Onset.

A gradual onset of anæmia, weakness, breathlessness, and palpitation, dating from about two years before he came under notice—without any obvious cause, and especially marked during the last twelve months. The only special symptoms were those connected with his stomach, namely, epigastric pain with tendency to nausea and retching, especially if stomach were empty; so that he was treated throughout as one suffering from chronic gastric catarrh.

On the top of these comparatively mild gastric symptoms there developed a degree of anæmia and weakness *out of all proportion* to the severity of any apparent cause, the anæmia so great that when he was first seen the corpuscles were reduced to 30 per cent., and his hæmoglobin to 35 per cent.

This relation of events—a history of antecedent gastric or intestinal trouble extending usually over many years, *more or less suddenly followed by a rapidly developing anæmia out of all proportion to the actual extent or severity of symptoms or lesions existing in the stomach or intestine*—such is, in my experience, the typical mode of

development of pernicious anæmia. This more or less suddenness of development, with the extraordinarily high degree of anæmia (exceeding anything ever met with even in the severest forms of wasting anæmia), are the clinical features which I have come to regard as denoting the supervention of a new factor—viz. definite infection of some part or other of the alimentary canal.

It is this history that leads me to inquire minutely into the character of the oral (especially tongue) symptoms at the very outset of the illness.

In the present case the account gathered from the patient is singularly clear. He had a history of oral sepsis extending back for ten years. At the very outset of his anæmia, he was greatly troubled with a "sore mouth," and I refer to the account itself for the remarkable history given of the persistency, painfulness, and above all *periodicity* of the glossitis there described, the attacks coming on every three weeks or so, accompanied by the gastric symptoms already referred to.

I shall again recur to the character of these tongue symptoms and their significance. For the present, what I wish to draw particular attention to is their *relation to the onset of the illness*—namely, they occurred as one of the first symptoms, when his anæmia and weakness were only commencing.

This is the point to which I recently drew attention ('Lancet,' January, 1900). As I have described in seven cases I have there recorded—

"*Mode of onset.*—The origin of the glossitis was in all cases as mysterious, and sometimes as sudden, as the weakness itself. The conditions were not simply the result of the anæmia. On the contrary, when they were of a character (by discomfort or painfulness) to attract the attention of the patient, they were always noticed at the onset of the disease or early in its course; and in most cases they actually subsided as the anæmia progressed. So closely connected were they, indeed, with the origin of the disease, that in three cases they were

among the first symptoms noticed and complained of; and in three cases the patients dated their weakness from the onset of the trouble in the mouth."

Additional Cases.

Since the foregoing was written in January, 1900, the following additional cases have been observed by me, and will serve to emphasise the points above mentioned with regard to relation to onset, characters, and periodicity of this characteristic glossitis.

Case 1 (the one now described).—Illness began two years ago; pallor, lemon-colour, constant pain in the stomach and side (over spleen), and periodical attacks of severe pain in the mouth and stomach. At this time he was greatly troubled with "a sore mouth." It began by pain and swelling of the gums; the teeth became to the feel sharp-edged, and felt as if they cut his tongue. In twenty-four hours after this the tongue itself became almost unbearably sore, and on examination showed big red patches on the dorsum and edges.

His tongue felt "as if it had no covering; as if it was quite raw, so that when I put a piece of bread in my mouth, it felt like sand-paper." The attack usually lasted two or three days, after which the patient could eat beefsteak or anything else. The attacks came on almost every three weeks, and were always followed or accompanied by gastric symptoms. This continued till Christmas, 1899. He had then three very bad teeth extracted, since which time the mouth condition has been considerably less.

Case 2.—"For a fortnight at onset of illness great soreness of tongue, necessitating use of a soothing mouth wash." A condition of extreme dental caries; only six good teeth remaining; ten rotten stumps in gums; other teeth absent. (A typical case of pernicious anæmia, with intense anæmia and urobilinuria.)

Case 3.—Ill-health began four years ago, end of 1896. In February, 1897, sore throat with considerable pain on swallowing, the pain seemed to run down into stomach. This lasted

for fourteen to twenty-one days, when it disappeared. Since then he has had slight attacks of sore throat at varying intervals up to the present time. End of 1897 first had trouble with his tongue, slightly swollen around the edges, with severe longish patches of a deep red colour, extremely tender. A few patches on the dorsum, less numerous and painful than those on the edges. Tongue very tender, especially to warm liquids. It got well in about a week's time. He has had repeated attacks of sore tongue since then, about once every two or three weeks, up till the last nine months, since which they have been slighter and at longer intervals (every two months). Since beginning of this year (1900) has hardly noticed anything wrong with his tongue.

On admission, tongue slightly red, with a few transverse cracks, edges rather glazed on the dorsum; not tender. Gums swollen and inflamed, projecting betwixt teeth. Teeth all in a very bad state of preservation, all the incisors and canines loose.

Under treatment with antiseptic mouth wash, redness of tongue rapidly disappeared. Seven weeks later tongue again became tender, red, showing small red granulations on its right edge. Temperature at same time rose a little; patient looked ill. This continued for nine days; then it lost its general red colour, but continued to show on its edges a number of angry red spots, size of a pin's head. (Death. Typical pigment changes.)

Case 4.—Three and a half months after illness began, patient noticed soreness of mouth and tongue. The degree of soreness has varied from time to time; at times the mouth causes no discomfort. During an attack the "tongue" "feels raw as if it had been cut." Dental caries and stomatitis. (Death from acute congestion of lungs. Typical pigment changes of pernicious anæmia in liver and kidneys, and bile.)

Case 5.—A lady æt. 39. Typical pernicious anæmia, as regards blood changes and characteristic grouping of features (hæmolytic, gastro-intestinal, nervous), I have above described.

At outset of illness, twelve months before, tongue very tender, necessitating soothing mouth wash.

The significance I attach to this glossitis is—

(1) It is not the result of the anæmia or weakness *per se*, for it often antedates the anæmia, or is most marked early in the disease.

(2) It is not an *ordinary* glossitis, such as is produced by ordinary oral sepsis. In the case now recorded, an attack occurred about a fortnight ago (February, 1901), notwithstanding that the patient's blood at the time showed 95 per cent. of corpuscles and 105 per cent. of hæmoglobin, and that there is no trace of oral sepsis.

(3) But it has special features, which denote that the tongue is the seat of a special infection which comes and goes, causing definite lesions. These lesions are at first small inflamed areas, denuded of epithelium, on sides or dorsum of tongue, sometimes showing angry red granulations, sometimes with formation of vesicles, sometimes resulting in linear cracks; in certain cases involving the whole tongue, so that it presents an angry red beefy look; in rare cases causing the tongue to swell up; in all cases resulting in atrophy of the mucosa, so that the tongue comes to present a very characteristic smooth polished appearance.

Another feature is its remarkable periodicity, coming and going in the most mysterious way independently of any obvious cause. This is, according to my observations, a notable character of every other clinical feature of the disease, even of the weakness itself.

Blood Changes.

On presenting himself the patient was found to have only 30 per cent. of red corpuscles, with 35 per cent. of hæmoglobin; that is, he had—

(1) A very high degree of oligocythæmia, far in excess of that producible by malignant disease alone, however long lasting, or by wasting disease; and produced without the intervention of hæmorrhage. This feature I regard

as highly characteristic of the blood change in pernicious anæmia; not distinctive in itself, if severe hæmorrhage have previously occurred, but highly distinctive when combined as it was in this case with—

(2) A relatively high hæmoglobin ratio of the individual corpuscles.

In my experience this high ratio is never met with in anæmia from loss of blood.

As I shall presently show, the diagnosis of the disease is not to be based upon the blood changes alone, but only upon these when taken in conjunction with the no less constant and characteristic groups of symptoms which I shall presently describe.

The chief significance I attach to this high degree of oligocythæmia is this:—In my judgment it denotes that hæmolysis is greatly increased, since according to my observations it is easy to produce the *highest degrees* of oligocythæmia by means of hæmolytic agents, while the experience of disease teaches clearly that this is not easy, even by repeated hæmorrhages, still less by wasting nutritional diseases, however profound.

Clinical Features.

As regards the *general* features which go to make up the clinical picture this disease presents, no description ever given can better the original one of Addison: a general anæmia occurring without any discoverable cause whatever; pursuing a similar course, and with scarcely a single exception, followed after a variable period by the same result; making its approach in so slow and insidious a manner that the patient can hardly fix a date to his earliest feeling of the languor which is shortly to become so extreme; increasing pallor; indisposition to exertion, with faintness or breathlessness on attempting it; bloodlessness of lips, gums, and tongue; failure of appetite, extreme languor and weakness, till the patient can no

longer rise from bed, and at length, sooner or later, falls into a prostrate and half-torpid state, in which he finally expires.

As regards the relation of these symptoms to one another, and to the anæmia, their essential feature appears at first sight to be, that one and all of them are referable to the anæmia. The latter appears "idiopathic, primary, essential, without any symptoms during life that cannot be explained as directly due to the anæmia" (Pye-Smith).

Even the *fever* so commonly met with appears to be "anæmic" in its character (Immermann); the *hæmorrhages*, likewise, are the result of fatty degeneration of the capillary walls, consequent on the anæmia; the *nervous disturbances*, psychical, sensory, or motor, such as are not infrequent, have been referred to the capillary bleedings in the nervous system (Eichhorst); and lastly, the *alimentary disturbances*, not infrequent, if only slight, seem merely results; if severe they appear to be possible aids in producing the disease, from the exhaustion and profound disturbances in nutrition they occasion (Biermer, Eichhorst, and Fenwick).

From the definition I have given it will be seen that, in the light of the foregoing studies, the various clinical features presented by the disease have, in my mind, assumed a somewhat different relation to one another.

I am accustomed to divide them into four groups, and these are well illustrated in the present case.

1. *General symptoms.*—A group which may be regarded as *effects* of the anæmia.

These include most of the more prominent features of the disease, such as *pallor, weakness, breathlessness, palpitation, irritability, sleeplessness, incapacity for mental or bodily exertion, want of appetite, feeble digestion, sluggish intestinal powers*, and lastly, the general normal *characters of the urine*, as regards quantity, excretion of urea, freedom from albumen, sugar, bile, blood.

Special symptoms. 2. *Hæmolytic.*—A group, the effect not of the anæmia itself, but of its *hæmolytic character.*

These include the *lemon colour*, varying greatly in intensity at different periods; the *urobilinuria*, with or without *high colour of the urine*, also varying greatly at different periods; occasionally also, deeply bile-stained fæces, likewise varying from time to time.

3. *Oral, gastric, and intestinal.*—A group related to the anæmia not as effect or as causes, but denoting *the site* of the lesion underlying the disease.

These include the *oral, gastric,* or *intestinal* symptoms, varying in intensity from time to time; insufficient of themselves to account for the anæmia; and not to be accounted for by any mere weakness resulting from the anæmia; but important as marking the existence of some special irritant trouble in the portions of the alimentary tract affected.

4. *Toxæmic.*—A group, like the last, neither cause nor effect of the anæmia *per se;* but denoting the toxic *character,* and infective nature of *the agencies* causing the anæmia.

These include most prominently of all, the *fever*—which comes and goes in the most varying manner, but is, in my opinion, rarely if ever absent in any case that is actually advancing. It also includes other phenomena, not so general but often met with, all of them characterised by the same periodicity which has been seen to be so common with most of the other features, namely, *headache, perspiration, drowsiness, languor, feelings of intense weakness,* and illness; also a group of more pronounced *nervous disturbances,* denoting actual lesions in central or peripheral nervous system, such as *pains, numbness,* and *tingling* in the arms and legs, *disturbances of sensibility, ataxic phenomena, loss of knee-jerk,* sometimes actual *peripheral palsies.*

It is the existence of all these groups of symptoms, in connection with a profound oligocythæmia, that consti-

tutes in my judgment the complete and characteristic clinical picture which this disease presents.

In my experience they are to be found in combination in every case of pernicious anæmia; they are all related to one another, although sometimes one or other may be specially prominent; and they have one marked feature in common, namely *periodicity*—the same feature which, as already seen, characterises the local lesions met with in the tongue.

In the present case these features were well exemplified.

Group 1.—General Clinical Features.

These I need not dwell upon. They comprise what are generally regarded as the chief, and by many the characteristic features of the disease, the symptoms for which the patient seeks advice—the weakness, breathlessness, palpitation, etc.

The relation between them and the poverty of blood seems obvious. They seem the direct result of the blood changes, and to be proportioned to these.

If they comprised, as they are held by many to comprise, the chief features of the disease, then the disease might apparently with reason be described as being without any symptoms other than those referable to the anæmia itself.

And yet with regard to many of these, I have to point out that they are only *in part*—not *wholly*—caused by the degree of anæmia present. That is to say, the weakness, lassitude, inability for exertion, breathlessness, palpitation, etc., are *not* always proportionate to the degree of anæmia present. On the contrary—

(1) *They may all be extremely marked, with a relatively good condition of blood;* and

(2) *They may all be absent, with a much poorer condition of blood.*

In other words, with regard even to these general features, *some other factor than mere degree of anæmia is at work.*

A patient may be *very ill* and weak, with over 60 per cent. of red corpuscles and hæmoglobin; while another may be actively going about and feeling well, with only one half that proportion. And even in the same patient at different times, he may be so ill that he can hardly walk or even sit up, with his blood showing 26 per cent. of corpuscles and 40 per cent. of hæmoglobin; and two months later he may be able to go about from morning to night, take walks, go up and down stairs, eat well, and describe himself as "feeling better than he had done for several years;" yet his blood show only 28 per cent. of corpuscles and 35 per cent. of hæmoglobin (Case 10, op. cit.).

I consider this a remarkable feature of the disease—one which demonstrates that the clinical features, even the simplest of them, are not referable to the degree of anæmia, and to that alone.

2. Hæmolytic Changes in the Urine.

These include high colour of the urine, marked by urobilinuria; the latter having, according to my observations (1889), certain special features which distinguish it from the urobilinuria of febrile disease.

Like all the other features this character of the urine is marked by *periodicity*. It is related to the degree of hæmolysis occurring, and this in turn to the activity of the infective process within the gastro-intestinal tract.

I show now samples of the urine from the case described from the time of admission, six months ago, up to the present time (January, 1901).

At the outset the colour was high.

It improved steadily, albeit slowly, for the first two weeks under his treatment; afterwards more markedly,

so that when he went out after five weeks it was of normal colour. It continued to vary for some time after; as the patient described it, "it was always darker when he was not feeling very well." It is now (January, 1901) pale and natural colour, although he possesses 104 per cent. of hæmoglobin and 90 per cent. of red corpuscles; whereas when his disease was in progress it was very dark, although he had only 35 per cent. of hæmoglobin and 30 per cent. of corpuscles.

This relation of urobilinuria to the general progress of the disease, and to the other clinical features (those comprised in Groups 1, 3, 4), I have brought out in a chart, which I now show, from another case which I had under continuous daily observation for some three months or more (see chart, op. cit.).

It can there be seen how closely the curve of urobilin followed the general progress of the disease; when the patient was well, the urine being almost colourless, so pale was it; while corresponding with his active attacks, characterised by sore tongue, vomiting, fever, lemon colour, and feelings of intense weakness, the urine was always higher in colour.

This relation of events was the feature I drew attention to in my original studies in 1889.

It is in my experience a very instructive one, if carefully observed over a period of time.

3. Oral, Gastric, and Intestinal Symptoms.

To the group of symptoms connected with the alimentary tract from the mouth downwards I attach a special interest and importance, and this not on account of their severity or persistence. The interest they have for me is their existence at all in connection with this tract. The basis of that interest is entirely pathological.

These gastric and intestinal symptoms have no other

characters than those recognised and described by the earliest observers of the disease; sometimes so severe as to appear to be the cause of the disease; sometimes so slight as to appear to be simple results of the anæmia. One would gather from the accounts they sometimes seem absent altogether, or so slight as to be not worth noting.

The facts which first drew my attention to this group of symptoms were those ascertained by the investigations I carried out between the years 1885—1888. The results of these, published in 1888, showed (1) that the blood change was essentially *hæmolytic;* (2) that this hæmolysis was originated and confined to the *portal area;* moreover (3) that this hæmolysis was of a *special character.* These facts pointed to the gastro-intestinal (portal) area as the seat of some special processes.

On *clinical grounds* alone there is no reason to attach to these symptoms—oral, gastric, and intestinal—any other significance or importance than was attached to them by all the earlier observers, and they include such notable clinicians and observers as Addison, Wilks, Biermer, Quincke, Immermann, Eichhorst, Pye-Smith, Bristowe, Bramwell, Coupland, and Mackenzie.

Addison made no mention of any such symptoms.

The occurrence of gastro-intestinal symptoms was noted by Biermer. He attached a double significance to them. If slight, they were effects of the anæmia. If severe, they were causes. "The most common cause was chronic diarrhœa, with or without gastric disturbance."

Following this teaching, almost all earlier observers attached a similar double importance to them. When severe, they were held to be themselves the cause of the disease; when insufficient to be accounted causes, they were regarded as effects (Eichhorst). This point I have brought out elsewhere (op. cit.).

And Dr. Pye-Smith, in his account of the disease in 1883, while referring to dyspeptic symptoms as common in the disease, evidently took a similar view of their im-

portance, since he defined the disease as "without any symptoms that could not be ascribed to the anæmia."

Significance.—The special significance I have been led —as *the result of my pathological studies*—to attach to these gastro-intestinal symptoms differs essentially from that above indicated. They do not, in my opinion, suggest the "gastro-intestinal origin," nor yet the "gastro-intestinal cause," nor yet the "gastro-intestinal nature" of the disease. Their significance is that they denote the *gastro-intestinal site of the infection causing the disease.* They derive their importance not from their severity, or their character, but from their existence at all in connection with this area.

As I have elsewhere shown, the symptoms of gastro-intestinal disturbance accompanying this anæmia include in the case of the *stomach* not only vomiting and diarrhœa, but almost every variety and degree of disturbance, *e. g.* indigestion, anorexia (sometimes alternating with ravenous appetite), nausea, sickness, pyrosis, salivation (rare), acidity, retching, vomiting, gastric pain, dilatation of the stomach with splashings, general discomfort over the stomach; in the case of the *intestine,* looseness of the bowels, diarrhœa, and colicky pains. And, as regards their frequency, an analysis I have made of a total of 279 recorded cases shows that the frequency of such symptoms is even greater than supposed, *mention* of gastric or intestinal symptoms being found in no fewer than 84 per cent. of cases.

The proportion might in my experience be increased up to 100 per cent., for they form a constant feature of every case *at some time or other,* although at times they may be in abeyance, or at most so slight in character as to be overlooked. As it happens, in the first case I observed and carefully studied, the absence of dyspeptic symptoms or gastric discomfort was a notable feature during the time he was under my observation. But they formed a prominent feature at one time before; and post

mortem I found evidences of subacute gastritis and atrophy of gastric glands.

Whether slight or severe they have an equal significance in my eyes. They stand to the disease in precisely the same relation as the intestinal symptoms stand to typhoid fever. They may be severe, as these latter may be; they may be moderate, as these latter may be; they may even be so much in abeyance as hardly to arrest attention at all, as the intestinal symptoms in typhoid fever may be. Yet all these variations are, in its case, as in the case of typhoid fever, compatible with the presence of lesions in the intestine—very obvious and definite in the case of typhoid fever; obscure and requiring to be sought for, but nevertheless there, in the case of pernicious anæmia.

As I have just said, the severity of this group of symptoms, indeed, varies much, both in different cases and in the same case at different times. This latter circumstance is of importance. A case may appear to be without symptoms of this kind at one time; yet at another later period, when the case is possibly not under observation, gastric or intestinal symptoms may be present. The important point about them in my judgment is, that they are not of sufficient severity or persistence to be themselves the cause of so grave and remarkable a form of anæmia, any more than the pain and discomfort of the throat or the slight fever can be adjudged to be the cause of the profound effects of diphtheria, or the gastric and intestinal symptoms in typhoid fever can be held accountable for the remarkable effects and course of that disease. They are mere symptoms. If very severe, *e. g.* vomiting, or diarrhœa, they of course, as in typhoid fever, add gravely to the exhaustion occasioned by the disease. Still, even then they are not the cause of the disease—pernicious anæmia,—they merely denote the site of the infection responsible for the disease.

In the case just described the gastric symptoms were prominent, and that, too, from an early stage of the

disease, as also the tongue symptoms, accompanied in their case by recognisable lesions which could be seen to come and go.

Pernicious Anæmia not a Gastro-intestinal Dyspepsia.

In this connection I may take occasion to correct an impression which prevails with certain writers with regard to the nature of these gastro-intestinal processes to which I attach importance. They are sometimes spoken of as if they were the result of some kind of gastro-intestinal dyspepsia.

I desire to draw attention to the fact that this is not my conception of the nature of the processes which give rise to the toxic substances responsible for the hæmolysis. They are the result of the special infection in the parts of the mucosa affected. Another misconception I may also take occasion to correct.

In the light of subsequent knowledge regarding the frequency of gastro-intestinal symptoms, I find it regarded by some as almost "natural" to conclude that the gastro-intestinal tract must be the seat of some special processes; that hence the portal area must "naturally" be the area specially affected by any increased hæmolysis produced by these "perverted intestinal processes;" and that consequently the liver must "naturally" show most evidence of this increased hæmolysis in the form of pigment.

I desire, however, to point out that the knowledge that thus seems "natural" was only arrived at after years of detailed work and experiment; that the order of progression of studies was precisely the reverse of that stated. It was, namely—

(1) Pigment changes in the liver.

(2) Portal site of hæmolysis.

(3) New significance attaching to gastro-intestinal processes.

In particular it took three years' work, involving many

experiments, to establish the fact that the portal area was the chief seat of hæmolysis, and thus to lay the pathological basis for the conclusion that the gastro-intestinal area was the site of the disease.

Infective nature.—The disease is not a special form of gastro-intestinal dyspepsia. It is the result of a definite infection of the mucosa, spreading from point to point, healing up in part, and then spreading to another. The special characters of the lesion can be best seen and studied, as in the present case, in the tongue—angry red patches, denuded of epithelium, on the dorsum of the tongue, followed by a smooth atrophied patch which persisted for weeks. And now that the disease is arrested, this patch has again become covered over with normal epithelium. But even now it shows from time to time signs of recurrence, denoting the deep-seated character of the infection *once it has taken root.*

4. Toxæmic Symptoms.

The class of symptoms I here designate "toxæmic" are those which, in my judgment, cannot be ascribed to the anæmia *per se*—*i. e.* to the actual poverty in corpuscles or in hæmoglobin; but denote rather the influence of other agencies of a *toxic character.* They all have one character in common—*periodicity.*

They really include many of the commonest and most characteristic features of the disease. That is to say, the intense feeling of illness and weakness which the patient experiences is not constant, but varies remarkably from time to time, sometimes even from day to day, independently of any recognisable changes in the blood sufficient to account for it.

The colour of the urine also changes periodically without any assignable cause.

The gastro-intestinal symptoms also display a no less marked periodicity. But the group of symptoms which I

desire to draw attention to by the special title "toxæmic," are those connected with the temperature and the nervous system—namely, *fever* and *nervous disturbances*. The symptoms connected with increased hæmolysis and gastro-intestinal irritation are evidences of more *local* disturbances—within the gastro-intestinal mucosa and the portal blood respectively. The fever and the nervous symptoms are evidences of more general and wide-spread disturbances.

Fever.—Fever is, in my experience, a notable feature of the disease, not so much from its character or its severity as from its existence at all. It is quite irregular in type, and very varying in degree. It may be, and often is, absent for considerable periods of time; but even in such cases it will be found that a slight rise of temperature at night—to between 99° and 100° F.—is the rule. Variations of a much more marked character occur from time to time, independently, apparently, of any cause. During these attacks all the other symptoms undergo exacerbation—namely, sense of illness and increase of weakness, increase of hæmolytic changes in the urine, occurrence of sickness or looseness of bowels —sometimes the one, sometimes the other predominating.

The fever is not always proportionate to the severity of the case, or the severity of the other characters of the disease. In other words, sometimes the *local*, at other times the *general* disturbances predominate. An interesting feature I have several times had occasion to observe is, that patients who have had a particularly sharp bout of high fever with general disturbance have often experienced a no less marked and sudden respite in the progress of their disease; whereas those who may be steadily losing ground may show only a slight rise of temperature.

These features are, I think, explained by the nature of the fever itself. It has been regarded as "anæmic" (Immermann), due to want of hæmoglobin, as "humoral" (Biermer).

My own view of it is that it is largely septic, and that all its characters find in this their fullest explanation, *e. g.* its irregularity, its slight degree when the disease is possibly advancing (denoting a total absence of power of reaction on the part of the body), or its occasional high degree, followed by rapid amelioration (denoting a sharp reaction on the part of the body).

Probably two factors co-operate to give it its irregular character: (1) the resistance of the body on the one hand; (2) the activity of the lesions on the alimentary mucosa and the toxic absorption on the other.

The gastro-intestinal irritation is due to the lesions themselves, the general toxic effects to the absorption. Even in health, with the blood normal, the effect of septic absorption on the temperature is variable enough, sometimes marked when the absorption is only slight, sometimes absent or slight when it is far greater.

In pernicious anæmia the blood is profoundly deteriorated, so that the wonder is that one ever gets a sharp reaction at all.

In the present case the fever was of the mild character (as will be seen in accompanying chart).

During the first five days its slight irregular character is well seen, varying from 97° to 99·6°; but during this time the blood had deteriorated by 3 per cent., and the urine was very dark, denoting active hæmolysis. The subsequent variations were connected with the serum injections, and it is to be noted how remarkably steady the temperature was at the period he was making rapid progress (adding 30 per cent. of corpuscles to his blood). After the last injection the temperature lost this steadiness somewhat, and it is interesting to note that the blood condition at this time remained stationary,—indeed, went slightly back.

Nervous Symptoms.

The other group of symptoms which I regard as specially toxic in origin are those connected with the

nervous system. They include not merely slighter effects, such as those I have mentioned, as intense sense of illness, weakness, utter exhaustion, but also more serious effects denoting actual affection of parts of the nervous system—sensory, motor, and trophic,—such as numbness, tingling, slight loss of power, actual paralysis.

The point of interest about them is that they occur at all; the degree of their intensity is a point of secondary importance.

In the present case they comprised numbness and tingling, and feeling of deadness in fingers, of which constant complaint was made (see history). Curiously enough they have proved the most persistent of all the symptoms. They still remain—after seven months—although they do not now give any trouble. The nature of the actual lesions associated with the severer forms of nervous affection in this disease is known to this Society from the very full account given by Dr. James Taylor in 1895.

The problem which this group of symptoms presents to me is the following (that they are toxic seems undoubted) :—Are they the effects of the special (hæmolytic) infection underlying the disease, or are they the effects of the antecedent and concurrent sepsis (oral and gastric), which in my experience is invariably associated with the disease ?

For reasons I have elsewhere given ('Practitioner,' December, 1900), I regard them as largely of the latter character; and for this reason, that I have found precisely similar nervous effects connected with extreme oral sepsis, and unattended by any anæmia.

The fact, however, that these nervous effects, in slighter or more marked degree, are met with so often in this disease—in my experience in at least two thirds or more of the cases—suggests that they may also be due partly to the special (hæmolytic) poison of the disease itself.

Treatment.

The conclusions I have formed regarding the infective nature and special seat of the infective process have suggested new lines of treatment with regard, (1) first, to the possible prevention, and (2) possible arrest of the disease after it has declared itself.

From this point of view the important point is not so much the actual character of the organism concerned as the site of the original infection—the mouth, and the part played in this infection by antecedent and concurrent oral sepsis.

In their order of importance the following are the lines of treatment to be followed out, all of them exemplified in the present case.

1. *Oral antisepsis.*—Complete in its character, both with regard to diseased teeth, irrespective of any absence of pain or discomfort such teeth may be causing, and to the special lesions of the tongue.

2. *Gastric and intestinal antisepsis,* in effecting which removal of the oral sepsis is one of the most important measures to be carried out.

3. *Arsenical treatment,* of whose great value there cannot be a doubt.

For the improved prognosis with regard to the disease—the average duration being now in my experience some three years—the use of arsenic deserves, in my judgment, the credit. It is no less certain, however, in my experience, that arsenic alone cannot permanently arrest the disease.

The disease has, with very rare exceptions, hitherto always recurred, and eventually killed. This may possibly be due to the remarkable persistence of the infection, well exemplified in the present case by the recurrence of the lesions in the tongue. It may, however, be due to the fact that hitherto, the infective nature and oral site of the infection in the first instance not having been recog-

nised, the patient cured once of his disease by arsenic has been left with the local septic conditions which originally favoured the infection, and favour either renewed infection or extension of the old. How persistent the infection is! This, I would fain hope, has been the case; it forms the most favourable element in regard to the future prognosis of the disease, and the present case forms in that respect the most favourable one I have yet seen. Future experience alone can decide upon it.

If these measures combined serve to avert the disease permanently—and of the two I attach greatest importance to complete oral and gastric antisepsis—there will be no need for any other treatment. But if they do not, the only measure is the one I have recommended of (4) *antitoxic treatment*, with the hope of thereby antagonising the poisons within the blood responsible for the hæmolysis.

In the present case the treatment adopted was—

Period 1.—Oral and intestinal antisepsis—carried out continuously over a period of seven months.

Period 2.—Antitoxic serum (streptococcic).

Two injections of 10 c.c.
„ „ 5 c.c.

given in a period of three weeks.

Result:

Corpuscles	+ 40 per cent. (67 per cent.).
Hæmoglobin	+ 37 per cent. (72 per cent.).
Weight	+ 1 lb.

General health.—Greatly improved. Hæmolysis arrested (urine very pale).

Period 3 (six weeks).—Sent to the country; arsenic still withheld. As a tonic, ʒj of syrup of hypophosphites.

Result:

Corpuscles	— 3 per cent. (64 per cent.).
Hæmoglobin	+ 8 per cent. (80 per cent.).
Weight	+ 6 lbs.

General health.—Much better.

PERIOD 4 (six weeks).—Medicine liquor arsenicalis ♏2½ ter die.

Result:

Corpuscles	+ 16 per cent. (80 per cent.).
Hæmoglobin	+ 10 per cent. (90 per cent.).
Weight	+ 16 lbs.

General health.—Very good; he looks in robust health.

PERIOD 5 (ten weeks).—Arsenic continued in ♏5 doses for six weeks, ♏2½ for four weeks.

Result:

Blood	+ 11 per cent. (91 per cent.).
Hæmoglobin	+ 14 per cent. (104 per cent.).
Weight	as before.

General health.—Robust, complexion high-coloured. Only symptom remaining is slight numbness at tips of fingers.

As regards the effects of the serum treatment, it was observed in this case, as in another case under my care, that the injection usually caused a distinct general reaction, lasting usually for forty-eight or sixty-four hours; and several times, as already stated, there was a local reaction as well; this latter, doubtless, due to some peculiarity of the serum employed.

Whether this reaction was connected with the character of the disease, or of the special serum used, it is impossible to state. But in view of its possible occurrence, it is, I think, advisable to begin with small doses (5 c.c.); and the precaution ought to be taken—as I have taken in the two cases I have had under my care—of (1) seeing that the temperature is not in an erratic condition at the time the injection is made; (2) strengthening the heart's action by means of ammonia and digitalis.

As regards the probable scope of usefulness of this treatment, it is at present quite impossible to speak. As I have said, the object of it is not to replace the line of treatment hitherto employed—and up to a certain point

successfully employed—namely, by arsenic; nor is it to replace the new line of treatment by combined oral and intestinal antisepsis, which I have recommended. To this latter I attach an even greater importance than to arsenical treatment, inasmuch as it aims at *the removal of the septic factor* associated with the origin of the disease—and of the infective lesions themselves.

It is intended to supplement both these lines of treatment if they fail to arrest the disease.

If both together fail to arrest the disease, this serum treatment appears to me to hold out prospect of benefit. And the case recorded—as also and still more the case recorded by Dr. Wm. Elder ('Lancet,' April, 1900), in which the blood condition rose from 16 per cent. of corpuscles and 24 per cent. of hæmoglobin, to 96 per cent. of corpuscles and 104 per cent. of hæmoglobin in forty-five days—certainly denotes that, carefully carried out, the serum has distinctly valuable therapeutic properties. In the present case the treatment was adopted early in the disease.

Should future experience show that complete antisepsis *plus* arsenic cannot arrest the disease, I should be disposed to carry out the serum treatment—not when the patient is at his worst, but in some period of partial arrest of the disease.

DISCUSSION.

Dr. C. Reissmann.—I should like to ask the author whether there are any special changes in the blood by which we can actually diagnose the nature of the mischief. There are cases which clinically appear to be pernicious anæmia, but which when examined post mortem show distinctly other changes. I have met with two cases during the last two years which showed all the changes usually associated with pernicious anæmia: the red corpuscles were reduced to two millions, many were nucleated, there was poikilocytosis, etc., yet post mortem we found colloid cancer of the stomach which was not even suspected during life. The patient had complained of pain in the stomach, but there was nothing to suggest malignant disease. The changes in the blood met with in association with pernicious anæmia are known to occur in other diseases,—for instance, in leucocythæmia. There the diagnosis is usually easy because there are certain changes in the white corpuscles, but apart from that the blood presents the typical appearances of pernicious anæmia.

Mr. T. J. Bokenham.—I propose to say a few words in contribution to the discussion of this evening's subject, and to approach the question not from the strictly theoretical side but from a clinico-pathological standpoint. Ever since we became acquainted with the fact that highly poisonous substances are constantly formed in the digestive tract as a result of the normal vital processes, and with the additional fact that the intestine is a regular hotbed of micro-organisms, it has been a subject of wonder how it is constantly becoming the victim of auto-intoxication or auto-infection. It has seemed reasonable to suppose that the liver, placed as it is between the blood from the digestive tract and that of the general circulation, must play some prominent part in our system of defence. There has been a certain amount of experimental evidence in support of such a view. More than twenty years ago Sir Lauder Brunton drew attention ('Pract.,' 1880) to the work of Lussana, Schiff, and others, who found that both organic and inorganic poisons, when absorbed from the intestines or introduced by a mesenteric vein, were separated by the liver, being excreted with the bile into the duodenum, and thus being prevented from entering direct into the general circulation. He pointed out the importance of this function in relation to poisons formed in the intestine during digestion. Further experiment has since shown that in relation to certain poisons, *e. g.* strychnine, quinine, veratrine, and morphine, the liver has the power of converting them

into harmless substances or else of storing them up temporarily and then re-excreting them so slowly that no toxic effects become manifest. We thought it quite possible that a further study of these functions of the liver might not only throw additional light on the question of immunity from auto-intoxication, but also on the larger ones of bacterial immunity and antitoxin production. I will now state as shortly as possible some very interesting results arrived at in the course of an experimental investigation conducted on these lines, results which, I think, are entitled to a place in this discussion. Working with livers isolated from the general circulation, and passing through them a "serum" containing either diphtheria or coli toxin (the latter prepared by Salimbeni's method), I found that both these toxins become so altered by, or stored up in, the liver that the outcoming fluid is deprived of a great part of its toxicity. Using a weak solution of indol, and causing it to circulate in like manner for some time through the liver, I obtained a fluid which no longer gave the "nitroso-indol" reaction, nor was I able by distilling from the liver substance to obtain a distillate giving a typical indol reaction. Passing now from toxic substances to living cultures of micro-organisms, I would first allude to the observation of Wissokowitsch, that when bacteria were introduced into the general circulation they rapidly disappeared from the blood, and were then to be found in the liver, spleen, and red marrow. He thought that they were ultimately eliminated with the bile. Werigo, too, has made very similar observations, and attributes the chief part in the arrest of microbes circulating in the blood to the endothelial cells lining the hepatic capillaries. It seemed to me worth while to extend observations in this direction, and with this object I injected very slowly a bouillon culture of *B. coli* (a culture of vigorous growth, but scarcely marked virulence) into one of the mesenteric veins of a cat. After a few moments I made plate cultures from (*a*) a superficial vein, (*b*) the supra-hepatic veins, and (*c*) the bile-duct. From the first nothing grew; from the other cultures only a few colonies were obtained. After half an hour the animal was killed, and cultures were made from the blood and liver substance. A sparse culture was obtained from the latter only, although sections of the liver showed the presence of large numbers of bacilli. Under these conditions it seemed, therefore, that the liver had acted not only as a filter but also as a destroyer of bacteria. In another experiment I injected the culture into a systemic vein. Here, again, the blood proved sterile, while the liver gave a limited growth. These observations seem, therefore, to confirm and amplify those of my predecessors, and that it is the liver which plays a very important part in protecting the circulation, both from toxic matters and bacteria.

When I repeated these experiments with a highly virulent coli culture my results were somewhat different. Injection into a superficial vein was followed by a rapid disappearance of microbes from the blood, but they reappeared after an interval, and death ultimately took place from septicæmia. Examination of the liver of an animal killed soon after injection showed, however, the presence of very numerous bacilli, so that even in this case there seems to have been an effort on the part of the organ to protect the body from general infection. In another experiment I therefore used an animal which had received previous injections of coli serum. In this case the result was exactly the same as when I used a non-virulent culture in a normal animal, as I proved both by the microscope and by culture. It looks as if the action of the coli serum had been to stimulate and strengthen the normal action of the endothelium of the hepatic capillaries. Perhaps at no distant period we may make use clinically of such a probable action of a specific serum in the treatment of certain auto-intoxications or auto-infections from the digestive tract. Finally, I would recall a suggestion which has often been made by Sir Lauder Brunton, that under certain circumstances the liver may so act as to remove certain protective substances from the blood, rendering the body even more than normally susceptible. We know how often a "cold" follows the use of calomel, although that drug is of undoubted benefit in removing the toxic substances which produce "biliousness." I am aware that another theory as to this susceptibility to cold after calomel is generally accepted, but I would submit that this "anti-antitoxic" theory is at least another possible explanation of its action.

Dr. S. Coupland.—We ought really to express the feeling which must animate us all of the extreme value of the service which the author has rendered to medicine by his patient and careful investigations into what has hitherto been regarded as a very mysterious malady. He has pretty well lifted the veil, and we now have a very fair notion of what pernicious anæmia really is. If I followed him correctly, the conclusion he seems to have arrived at is that pernicious anæmia is a hæmolytic disease excited by a specific poison which operates through the portal system, and that this specific poison only acts when the way is prepared for it by septic infection of the alimentary tract. It only remains for him to demonstrate the true nature of the specific poison, and, perhaps, to isolate the bacterium which is responsible for this mischief. That there must be a special poison (whether bacterial or not is immaterial) must surely be evident when we consider how rare pernicious anæmia is, and how common, alas! is oral sepsis. Dental surgeons could produce thousands of cases of this condition of the teeth and mouth for one of pernicious anæmia which a physician may show.

That, I imagine, is the position to which Dr. Hunter has now brought us.

Dr. SAVILL.—As regards the clinical aspect of pernicious anæmia, I think that we might with advantage reconsider the question of its position in nosology. Among my out-patients at the Hospital for Nervous Diseases quite three quarters come complaining of symptoms which we regard as neurasthenic, and a large number of these are of a vaso-motor kind. I have not taken the pains to observe with great accuracy whether they have had anæmia or not, but my impression is that a very large number of these cases were anæmic, and many presented the earthy complexion so common in dyspepsia, from which many of them suffer also. Their urine might be examined for hæmolysis, and thus possibly they might be brought within the category of this disease. In a word, I am inclined to think that the condition under consideration is by no means as rare as it was formerly thought to be. Of course one has always looked upon pernicious anæmia, prior to the researches of Dr. Hunter and others, as a severe and almost necessarily fatal disease, occurring chiefly in old men, but I see no reason why the cases I have referred to should not be of the same nature, only slighter in degree. The commonest cause of these neurasthenic cases is undoubtedly dental defect of some kind; a large number of them have suppuration going on in the mouth, and the cure of these cases rests largely with the dentist. I think, therefore, there is a very large field which might profitably be investigated from this point of view.

Mr. A. BARKER.—The investigations which the author has brought before us to-night have a great interest for surgeons as well as for physicians. First I would thank him for having drawn my attention to a very important subject, viz. the examination of the state of the mouth and tongue in certain conditions. Honestly, I feel almost ashamed, for I am obliged to say that I saw that specimen to-night for the first time, though it was taken from one of my patients. I was not aware that during life he had anything wrong with his mouth. He had suffered from a very serious gastro-intestinal condition, and he was nearly moribund when Dr. Hunter saw him first. In future, I shall certainly not allow any case like this one to pass through my hands without most careful examination of the mouth, and examining it in a way it has not hitherto been examined. He has shown us how very scrupulous we should be in certifying the fact that the condition of the mouth will produce profound anæmia and depression of vital energy, though in surgical cases that has been known to us for many years; indeed, for some years past we have been accustomed to endeavour to treat all cases in which we were going to operate upon the mouth in the direction of antisepsis, but I do not think we have realised how

the state of the mouth can contribute to the production of specific diseases of the intestine and stomach. The question, indeed, appears to me to be as interesting to surgeons as to physicians. In that case of mine, I believe the author was led to search in the man's mouth and frontal sinuses by a process of reasoning based upon the condition of the liver, spleen, stomach, and intestine, a thing which it had not occurred to us to do.

Dr. W. HUNTER —I am certainly indebted to Mr. Barker for one of the most valuable proofs I have had in my investigation of these cases. His case came within a month of my first article on this matter, and it was my first post-mortem. I think that one of his colleagues proceeded to examine the mouth. The front teeth were beautiful, but the back teeth were in the condition I have described. There was no obvious sign of trouble, but very marked pallor. Then I cut out the jaw and found an alveolar abscess. I wanted to examine the eyes, and on taking off the orbital plate a lot of pus oozed out. Of this condition of sepsis there was no suspicion during life. My conclusions are based on seven cases, now raised to ten, which all show clearly the connection between the morbid phenomena and the symptoms. I am very indebted to Dr. Coupland. In my paper I have thought it necessary to apologise for having ventured to come to such a different conclusion respecting pernicious anæmia from my predecessors, Dr. Coupland, whose great lectures on anæmia formed for a long time the basis of our knowledge, Sir W. Broadbent, and others. If I attached importance to any group of features to which they did not attach importance, it is for the reason that my pathological studies had given a basis to this gastro-intestinal condition which did not exist before. No one can attach to the condition of the mouth or tongue such as I have described any importance whatever on purely clinical grounds. Since this view has been brought forward, the term "gastro-intestinal" has been used in quite an unwarrantable manner, as if, indeed, pernicious anæmia were a mere gastro-intestinal disturbance. The condition of the gastro-intestinal tract is not the cause of the anæmia, but the result of the lesions which produce the anæmia, *i. e.* they tend to pernicious anæmia in the same relation as the lesions of typhoid fever or diphtheria do to the disease, but in no other way. I repudiate having formulated any gastro-intestinal hypothesis of the production of pernicious anæmia. The diagnosis of this disease is not to be based upon the blood-changes alone, but upon the blood-changes in association with four groups of clinical features which are as definite and as constant as that in connection with any other disease with which we are acquainted, viz. (1) anæmia, (2) changes in the character of the urine, (3) gastro-intestinal symptoms, and (4) general

effects, fever, etc., showing the effects of toxic absorption; and in connection with this there are a group of nervous lesions. I should be quite willing to exclude any case in which these four groups of symptoms were not present. A few months ago my attention was called to a case in which there was a history of suppuration of the jaws, and which had been diagnosed as pernicious anæmia. There was even a history of numbness and tingling of the fingers, yet, on examining that patient, the urine was perfectly pale and contained a slight trace of albumen. That patient died two months later from uræmic coma. In the paper I have shown that the streptococcus is only an associated organism, and I attach importance to it merely because it ought not to be there. I have shown that the streptococcus is not hæmolytic, and so far I know nothing of the nature of the special organism involved. It is a difficult task to isolate a particular organism in the mouth and stomach, but now we have traced the lesion back to the tongue perhaps we may be able to do something more.

THE PROGNOSIS AND TREATMENT OF CASES

OF

ASCITES OCCURRING IN THE COURSE OF ALCOHOLIC CIRRHOSIS OF THE LIVER

WITH

SPECIAL REFERENCE TO THE TREATMENT BY OPERATION

BY

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THERE is at the present time a considerable want of unanimity regarding the prognosis of cirrhosis of the liver after the appearance of ascites. Formerly all such cases seem to have been looked upon as hopeless, but at the present day, while their extreme gravity is fully recognised, a somewhat more hopeful view is taken of them, based upon the fact that a number of cases have been recorded in which the ascites has temporarily, or even permanently, disappeared after tapping.

Dr. W. B. Cheadle, in his recent Lumleian Lectures, has shown that much of the confusion regarding cirrhosis of the liver has arisen from a failure to differentiate

between their several types and stages. It is, as Dr. Cheadle clearly shows, of great importance to distinguish the different stages and varieties if any real advance is to be made; and it seems to me that this importance has become still more imperative, in face of the fact that an operation for "cirrhosis of the liver" has recently been introduced, an operation which will probably meet with but little success unless the cases are carefully selected.

The subject is a wide one, and necessarily somewhat difficult to summarise; but I have endeavoured to collect information from the works of others, and from my own experience, which will, I hope, among other things show the following points:

A. That ascites, arising during the course of a case of alcoholic cirrhosis of the liver, may be due either (1) directly to the cirrhosis, or (2) may depend upon some condition co-existing with the cirrhosis.

B. That ascites, when directly dependent upon the cirrhosis, is almost always a fatal symptom; while, on the other hand, ascites associated with cirrhosis, but not directly dependent upon it, may often be temporarily relieved, and not unfrequently cured.

C. That, under these circumstances, laparotomy, performed on cases of cirrhosis of the liver with ascites, is only likely to be successful in those cases in which the ascites is an associated condition of the cirrhosis, and not directly dependent upon it, and that, if this is so, it would seem misleading to look upon the operation as being one for the cure of cirrhosis of the liver; it should rather be looked upon as one for the relief of cases of ascites, some of which, although occurring in the course of cirrhosis of the liver, may still be amenable to treatment.

In the first place it will, I suppose, be granted by everyone that the condition of cirrhosis itself cannot be cured, *i. e.* the connective tissue when once formed cannot be got rid of by drugs, or any other means at our

disposal. That an advanced condition of cirrhosis may remain latent is true, and that it may become arrested is possible; but it cannot be cured. The question then arises as to how far symptoms may be relieved, and especially the ascites, which is frequently the first thing which causes the patient to seek advice.

The recoveries, which have taken place after the onset of ascites, are attributed to a development of the collateral circulation, whereby the blood in the portal veins finds its way directly into the systemic circulation, without passing through the liver, and, on this supposition, the usual custom in cases of ascites associated with alcoholic cirrhosis is to give a guarded prognosis, always bearing in mind that in a certain small percentage of patients the ascites disappears after tapping.

That patients recover from ascites, which *clinically appears to be due* to cirrhosis of the liver, is perfectly true, and it is equally true that recoveries take place from ascites *associated with* cirrhosis, but it is probable that it is only very rarely indeed that recoveries take place when the ascites is *directly due* to the cirrhosis.

This certainly seems to have been the view held by authorities a few years ago. In Reynolds' 'System of Medicine' the following passage occurs:—"It is probable that in patients in whom very free collateral circulation is established the progress may be slower, as cases are on record in which ascites has disappeared when the various venous anastomoses have been largely formed. It is possible, in such cases of free restoration of circulation by means of collateral channels, if the uninjured portion of the liver be sufficient for the purposes of life and the atrophy arrested, that existence may be maintained; *but there does not appear to be good evidence of such cases and results having occurred.*"

Dr. Bristowe, in speaking of cases of cured ascites ('Trans. Clin. Soc.,' vol. ii), clearly recognises the ascites which may be associated with cirrhosis from that which is directly due to it, for he says:—"We have reason,

therefore, to believe that the ascites which appears in the course of cirrhosis and such like diseases of the liver, may occasionally be immediately due to the superaddition of some remediable morbid condition, and may disappear temporarily or permanently with the removal of that condition, even though the hepatic disease be still progressing towards its inevitable fatal termination."

More recently a valuable contribution to the subject has been made by Dr. Hale White ("The Causes and Prognosis of Ascites," 'Guy's Hosp. Reports,' 1892), who found that many cases of ascites which during life were thought to be due to hepatic cirrhosis, were proved after death to depend upon something quite different, and in others which were tapped frequently there was some other cause present besides the cirrhosis which would account for the ascites, the most frequent being chronic peritonitis and perihepatitis.

Dr. Hale White concluded that when ascites depends upon cirrhosis of the liver, the patient rarely lives long enough to survive more than one tapping, and he published thirty-four cases illustrating these points.

Ten suffered from cirrhosis with ascites, and died before tapping was necessary; the average duration of life after the abdomen was first noticed to be enlarging was only eight weeks.

Fourteen were undoubted cases of cirrhosis, in which paracentesis was performed, and not one of them survived the first tapping long enough to render a second tapping necessary, and in not one was there any evidence that the tapping was beneficial.

Ten cases were regarded during life as having cirrhosis and tapped more than once; of these the diagnosis proved to be wrong in four, while the remaining six had chronic peritonitis associated with the cirrhosis. Dr. Hale White's teaching upon this subject is, I think, so generally accepted that it scarcely needs any corroboration; but, as I have made a number of post-mortem examinations upon cases of cirrhosis during the past two and

a half years, I have collected them, and also looked up some others from the post-mortem records of the Middlesex Hospital, making altogether eighteen cases, and on referring to their clinical histories the seriousness of the disease is well seen, and their results in every way support Dr. Hale White's conclusions. Twelve of the eighteen died before tapping was necessary, or soon after it had been performed once. Six survived more than one tapping, and in these, with the possible exception of one, there was adequate cause for the ascites in addition to the cirrhosis. The cases which only survived one tapping ran a very similar course to those recorded by Dr. Hale White, dying within a few weeks of the onset of the ascites.

When the ascites is associated with the cirrhosis, but not directly due to it, the prognosis, as far as the ascites is concerned, depends upon the stage of the cirrhosis at which it arises. It would seem that the associated ascites in cases of cirrhosis is also usually a late symptom, which accounts for the great fatality of this condition, which, although considerably less than in the cases which are dependent directly upon the cirrhosis, is still great, only a case here and there doing well for any length of time.

The results of post-mortem examinations show that the cases of ascites which, during life, appear to be due to cirrhosis of the liver, may be divided into three groups :

1. Those in which the diagnosis of cirrhosis is erroneous, the ascites being found after death to be due to some entirely different cause.

2. Those in which ascites is associated with cirrhosis, but actually due to some other cause.

3. Those in which the ascites is directly dependent upon the cirrhosis.

1. The first division of this group need not now be considered except for the purpose of emphasising the necessity of basing the evidence of cures upon ultimate post-mortem examinations. The liabilities of making

errors in the diagnosis of the causes of ascites are very great, and as an example a case recorded by Dr. Ewart may be mentioned, in which the patient was tapped fifty-two times, and also had laparotomy performed, on the supposition, which was proved afterwards to be erroneous, that the ascites was due to cirrhosis.

2. The commonest cause of ascites associated but not directly dependent upon cirrhosis of the liver is undoubtedly chronic peritonitis and perihepatitis. Dr. Hale White's cases show this, and my own post-mortem experiences fully support the frequent association of this condition.

Dr. Bristowe, in discussing the causes of ascites (Reynolds' 'System of Medicine'), alludes to the part which changes in the capsule of the liver play as follows:— "This formation, which is probably of inflammatory origin, is sometimes associated with cirrhosis or other morbid states of the liver, but is sometimes present when the liver seems otherwise perfectly healthy, and where it is the sole visible pathological phenomenon associated with ascites."

It may, then, I think, be fairly considered that the ascites associated with latent cirrhosis is very frequently due to these conditions.

3. The third group comprises those cases in which the ascites directly depends upon the cirrhosis, and the prognosis here appears to be very bad, the majority of cases dying within a few weeks after ascites has first been noticed. The average duration of life after the onset of ascites in Dr. Hale White's cases was only two months, and the collection of cases which I have made shows an equally grave prognosis.

Indeed, many cases of cirrhosis die before tapping becomes necessary, and out of 46 cases in which cirrhosis was discovered after death in 20 only was there more or less accumulation of ascitic fluid (Bristowe), facts which all point to ascites being a late symptom.

If then it is recognised that ascites is frequently pro

duced by chronic peritonitis and perihepatitis, it is no proof of the curability of ascites due to cirrhosis to cite cases in which these conditions are present. In order to prove the curability of ascites due directly to cirrhosis, post-mortem evidence must be obtained of uncomplicated cases of cirrhosis which have been tapped one or more times at some date previously, and afterwards lived in good health.

Such cases no doubt do occasionally occur, but I think they must be extremely rare, and considered as exceptions which in no way alter the general aspect of the question. Personally, during the time that I have been Pathologist at the Middlesex Hospital I have never met with such a case.

Dr. W. B. Cheadle has recorded in his recent lectures five cases which he has met with as examples of great improvement in atrophic cirrhosis. One of these was eventually lost sight of, and therefore cannot be regarded as a proved case. Of the remaining four, upon which post-mortem examinations were ultimately made, the following are brief extracts of the conditions present:

(1) F—, aged 53, admitted with ascites and hæmatemesis, tapped twice, and left hospital in two months free from ascites. Nine months later was readmitted with ascites, and was tapped. No return of ascites, but had a severe attack of pleuro-pneumonia, from which she recovered, but died a month later from acute bronchitis.

P.M.—Typically hobnailed, cirrhotic liver, weighing 38 oz., with thickened capsule, but no general perihepatitis or peritonitis; no thickening of, or adhesions to, neighbouring structures.

(2) M—, aged 43, died a year and a half after first coming under treatment for ascites.

P.M.—The cirrhotic liver was covered with thick false membrane.

(3) F—, survived first treatment of ascites one and a half years. Tapped four times.

P.M.—Abundant adhesions between liver and neighbouring organs.

(4) M—, aged 85, tapped eleven times, and also had laparotomy performed.

P.M.—Atrophic cirrhosis. Perihepatitis present.

On examining these four cases it will be seen that in three of them at least there were signs of perihepatitis and peritonitis, which therefore may have caused the ascites. In No. 2 the liver was covered with a thick false membrane; in No. 3 there were abundant adhesions between liver and neighbouring organs; and in No. 4 definite perihepatitis is recorded.

In No. 1, on the other hand, there does not appear to have been any cause for the ascites except the cirrhosis, and it appears to be one of the exceptional examples of a temporary recovery.

Dr. Hawkins, in the article on cirrhosis in Allbutt's 'System of Medicine,' concludes that after ascites has set in "the conditions necessary for the restoration of health must be very rarely attained."

The clinical course of cirrhosis of the liver may then, I think, be summed up as follows:

Cases may exist for years without any ascites, or, indeed, without any definite symptoms, but during this period ascites is liable to arise from some associated condition, the most common being chronic peritonitis and perihepatitis. Ascites arising from this cause may be frequently relieved, and occasionally it eventually entirely disappears, and the patient then returns to his former state of latent cirrhosis without any ascites. As time goes on the cirrhosis progresses until frequently it itself gives rise to ascites, for which tapping is of no avail, and the patient succumbs a few weeks after its onset.

Of course, there need not be, and frequently is not, any long interval between the first and last tapping, as the associated ascites often merges imperceptibly into that directly dependent upon the cirrhosis. Examples of these are to be found in cases which are tapped

repeatedly and survive a few months. In fact, all stages may be frequently seen except that of an uncomplicated cirrhosis which has survived several tappings and recovered, and there is but little post-mortem evidence of the occurrence of this condition. This view would also seem to be in harmony with clinical experience regarding the difference in the prognosis of ascites in large and small livers. Dr. Cheadle in discussing prognosis says, "To put it broadly, and speaking clinically, the cases which do well are those in which the liver, apparently large, exposes a flat, hard surface to the abdominal front, extending far below the edge of the ribs and sometimes down to the umbilicus." Now it is precisely in these large livers, which are almost certainly in many cases the early stages of the smaller ones, and therefore presumably in an early stage of the disease, that the ascites is more likely in many cases to be due to an associated condition, and not in that early stage so likely to be directly dependent upon the cirrhosis; and this being so, cases of ascites with large livers would be likely to do better than those with small livers, which, as already stated, Dr. Cheadle has shown to be the case.

Treatment.

The treatment of the later stages of cirrhosis of the liver consists chiefly in attempting to relieve the ascites, which can in most cases only be effectually done by tapping.

Formerly it was always considered wise to put off tapping as long as possible, now it is generally advised to tap early. This diversity of opinion has no doubt arisen from a confusion as to the actual causes of the ascites, some cases being benefited by this treatment and others not.

Without, however, going further into the question as to whether tapping should be performed early or late, it may

at once be stated that there is no good evidence to show that tapping is of any benefit in those cases where the ascites is directly dependent upon the cirrhosis.

Dr Hale White found that in fourteen cases the length of life after tapping was usually only a few days (the shortest was two days, the longest forty), and, as already stated, this group of cases seldom live long enough to require tapping more than once or twice.

Recently a more radical operation has been introduced with a view of curing cases of cirrhosis with ascites. First introduced into this country by Morison and Rutherford,[1] the operation consists briefly in opening the abdomen and promoting adhesions between the peritoneum, the omentum, and parietes, the idea being to establish a free collateral circulation which shall relieve the portal system and so prevent the recurrence of ascites.

This method of treatment has met with a certain amount of success, and I append a table of those cases which I have been able to find particulars of.

I have adopted the following table of operations chiefly from a paper by Frazier,[2] but have made various additions to the details where I have been able to find them.

It is very difficult to draw any definite conclusions from this table, since the cases operated upon are so various, and often otherwise complicated. It is, indeed, rather a table of operations for ascites from various causes, than one in which the ascites can be said to be due to cirrhosis. For instance, in No. 4 there was an ovarian cyst, and in No. 7 there was parenchymatous nephritis. If, however, we consider for the moment that these cases represent the general run of clinical cases, which are diagnosed as cirrhosis with ascites, it will be interesting to see how the results compare with those of tapping.

In this table we have, out of fourteen cases, four

[1] 'Brit. Med. Journ.,' Sept. 19th, 1896.
[2] 'American Journ. Med. Sc.,' Dec., 1900.

Table of Cases operated upon for Ascites due to Cirrhosis of Liver.

No.	Operator.	Age.	Sex.	Previous history and conditions found at operation.	Result.	Remarks.
1	Drummond and Morison	42	F.	Liver enlarged, pale, smooth, but not harder than normal	Recovery from operation. Recurrence of ascites	Required frequent tappings (69 times between date of operation and death). Died 19 months after operation. No P.M.
2	Drummond and Morison	39	F.	Was tapped frequently before operation; liver found to be "typically cirrhotic"	Recovered. No return of ascites	Perfectly well at end of two years. Finally died after an operation for ventral hernia. P.M.—Adhesions with vessels, some of them of large size, passing between omentum and viscera to parietes; liver atrophic and degenerated; spleen about four times its natural size.
3	Morison	42	M.	Illness of about 8 weeks' duration. Liver cirrhotic, but not so contracted as expected; spleen enlarged	Recovered. No return of ascites	Was known to be quite well 2 years after.
4	Morison	54	M.	Cirrhosis of liver; enlargement of spleen; ovarian cyst	Died	P.M.—A partial examination showed patient to have contracted kidneys.
5	Schelky	—	—	—	Died	Died of delirium tremens.
6	Lens	61	M.	Liver atrophic	Recovered. Ascites recurred	Was tapped five times before death, which occurred 6 months after operation.
7	Talma	9	M.	Liver enlarged, surface granular; splenic enlargement; parenchymatous nephritis	Recovered. No recurrence of ascites	The patient was perfectly well 26 months after operation.

No.	Operator.	Age.	Sex.	Previous history and conditions found at operation.	Result.	Remarks.
8	Neuman	45	M.	Enlargement of spleen	Recovered. No recurrence of ascites 6 months after operation	—
9	Weir	39	M.	Liver capsule thickened; spleen bound down by adhesions	Died on 5th day after operation	Purulent peritonitis.
10	Rolleston and Turner	52	M.	Ascites 2 months' duration; tapped twice before operation; liver markedly cirrhosed	Recovered. Recurrence of ascites requiring frequent tapping	When heard of about 4 months afterwards was ill in bed with distended abdomen and œdema of legs.
11	Rolleston and Turner	45	M.	Œdema of feet and ascites of about a month's duration, preceded by hæmatemesis; liver markedly hobnailed, but free from adhesions; peritoneum much injected	Recovered. Remained much improved. Four months after there was, however, a trace of ascites and some œdema of feet	—
12	Bossowski	9	F.	Liver cirrhotic	Recovered. Recurrence of ascites	The recurrence of the ascites appeared to take place less rapidly after the operation.
13	Frazier	45	M.	Liver cirrhotic; omentum short and thickened	Recovered. Recurrence of ascites for a time	The patient required tapping twice after the operation, after that there was no return of ascites at the end of 3 months.
14	Vande Meule	—	—	—	Died	—

which may be regarded as cured of the ascites, or, at any rate, very greatly benefited; they are Morison's cases (Nos. 2 and 3, both of which were well two years after); Talma's case (No. 7, well twenty-six months after); and Neuman's case (No. 8, no recurrence of ascites six months after operation; while two others (No. 11, Rolleston and Turner, and No. 14, Frazier) appear to have been considerably improved, but cannot be regarded as cured, since in one (Turner and Rolleston) there were definite traces of ascites and œdema of the feet four months after, and in Frazier's case the patient required tapping twice after the operation, and the record of freedom from ascites only extends for three months.[1]

In making a comparison with tapping, it must be remembered that many cases which are operated upon, are those which have already survived several tappings; and therefore, as already shown in the first part of this paper, are to a large extent removed from the more serious group, which die after the first tapping, and, further, it must be remembered that successful cases are more likely to be recorded than unsuccessful ones.

If now we take the records of a similar set of clinical cases, diagnosed as cirrhosis and ascites like the above, without any attempt to further classify them into the groups I have previously mentioned, we shall similarly find a considerable number of cases greatly relieved, and a few that have quite recovered. Dr. Cheadle, for instance, quotes eleven cases, in which recovery was either temporary or prolonged, exclusive of those in

[1] Since the above was written a paper on the subject has appeared by Drs. Packard and Le Conte ('Amer. Journ. Med. Sc.,' March, 1901), in which 22 cases have been collected. Two of these are recorded by the authors. One, a man aged 63, after repeated tappings, was operated upon on October 13th, 1900. He made an uneventful recovery from the operation, but gradually lost ground, and died on December 5th, 1900. The second case was that of a man aged 52, admitted into hospital September 7th, 1900, with an enormously distended abdomen. He was tapped on September 11th, but as the fluid re-accumulated rapidly he was operated upon on October 13th, 1900. He died on the 17th, four days after operation.

which there was mere relief of symptoms sufficient to admit of discharge from hospital, or private cases which were not traced afterwards, which is a very large percentage, and one which I venture to think will compare very favourably with the statistics of cases operated upon.

Those who consider the operation as one for cirrhosis of the liver look upon the ascites as being due to mechanical causes, and capable of being relieved by the establishment of a free collateral circulation. There are, however, good reasons for believing that the occurrence of ascites is not capable of such a simple explanation, and it is thought by many that it may be due to a toxæmia, which accompanies the later stages of the disease. That there is congestion of the portal system in cirrhosis there can be no doubt, as evidenced by hæmorrhages and frequent enlargement of veins; but that it will explain many of the later symptoms, including the ascites, is not so certain.

Moreover, there does not seem to be any evidence at present that the operation has been successful in an uncomplicated case of cirrhosis with ascites. Morison advises operation after one or two tappings; in his conclusions regarding the operation he says:—"It is no longer advisable to treat the cirrhosis by repeated tappings if the patient is otherwise sound and in fair general condition. After one or two tappings have failed, operation offers the best chance of prolonged and useful life."

Frazier considers the chief indication for the operation to be the presence of ascites due to obstruction of the veins of the portal system, when the obstruction itself is due to cirrhosis of the liver, but qualifies this later on by stating that the cases, which should be operated upon, are those to which paracentesis has failed to give relief.

Another view suggested by Rolleston is that the operation gives relief by affording increased nutrition to the liver and promoting hyperplasia of the cells, and, on this ground, he thinks that operative interference would

probably succeed better in the pre-ascitic stages than in the later ones ; but considering how long the disease may remain latent, and the uncertainties of its course, this suggestion is scarcely practicable.

There is, however, I think one other possible explanation, simpler than both the above, and that is, that the beneficial effects which follow the operation are simply due to the formation of adhesions between the two layers of the peritoneum, and so leading to obliteration of its cavity. This would, in itself, be sufficient to account for the non-return of ascites, without any necessity for explaining it either by the development of a collateral circulation, or by increased nutrition of the liver cells, both of which would require very strong evidence of their existence before they can be accepted as facts.

Obliteration of the peritoneal cavity, partial or complete, is not unfrequently seen in the course of tuberculous peritonitis, and the same process of obliteration, of course, often occurs in connection with the pleura and pericardium.

An interesting case, in which obliteration of the peritoneal cavity apparently occurred after tapping, has been recorded by Dr. Cayley ('Middlesex Hosp. Journ.,' March, 1897), and may be mentioned here. The patient, a cabman, was suffering from alcoholic cirrhosis and ascites, and was tapped fourteen times. After the last tapping some symptoms of peritonitis appeared, and the fluid did not again collect. He was discharged convalescent, and although his ultimate condition is not known, he was seen by Dr. Cayley well and driving his cab two years afterwards. In commenting upon this case, Dr. Cayley suggests the possibility of relieving ascites by exciting adhesive peritonitis, as often happens in cases of ascites due to tuberculous peritonitis.

If the operation is to survive, it must be shown that it possesses some distinct superiority over tapping, since, notwithstanding the slight risk of abdominal explorations, it is in every way more formidable than tapping, and it

must always be remembered that many of the cases which require it are neither good subjects for operation nor anæsthetic.

From what has already been said, it will, I think, be gathered that the cases best suited for operation are those in which the ascites is only an associated condition of the cirrhosis; the presence of cirrhosis is, of course, not by any means necessarily a contra-indication, but the further advanced the cirrhosis, the less chance must there be of the operation being successful; and if there is good reason to believe that active symptoms of cirrhosis have supervened, and that the ascites is *directly* dependent upon the cirrhosis, the operation should not be undertaken, for at this stage, putting the cause of the ascites on one side, the liver is nearly always in such a condition as to be incompatible with prolongation of life.

There must, of course, often be great difficulty in deciding whether the cirrhosis is still latent, and to this end the most careful attention must be given to the general condition of the patient, and any signs that may denote that the liver cells are not performing their functions well. Errors, however, will be further eliminated by only selecting such cases for operation which have been tapped several times, and so looking upon the operation as one likely to relieve some cases of ascites associated with cirrhosis of the liver, and not as one directed towards the actual liver condition itself; but the operation should not, it seems to me, ever be substituted in the first place for the more simple method of removing the fluid by tapping.

DISCUSSION.

Dr. PARKES WEBER.—Most cases I presume are tapped at least once before laparotomy is resorted to, and in this connection I wish to point out that if the specific gravity of the ascitic fluid is high, say up to 1020, which is very high, some inflammatory process may be supposed to be present. In such cases it would not be right to attribute the good result to the laparotomy, since there was clear evidence of previous inflammation, which might of itself have been sufficient with ordinary tapping to procure permanent or temporary cure of the ascites. Unfortunately, the estimation of the specific gravity of the ascitic fluid is very frequently neglected, and this must be remembered in considering the apparent results of surgical interference. In the case of cirrhosis to which I referred in the discussion [1] on Dr. Rolleston's communication to the Medical Society, the patient had to be tapped twice, and the specific gravity of the fluid was noted as 1020. At that time there was practically no doubt that he had cirrhosis of the liver, and this was confirmed by the result; yet no further paracentesis was required. When he died six years later I had an opportunity of seeing the condition of things; besides the cirrhosis of the liver there had been perihepatitis and perisplenitis. In similar cases if laparotomy were performed, the existence of a localised inflammation between the liver and diaphragm or around the spleen might escape notice, and the cure would then be set down to the operation. I think that when peritoneal effusion occurs *early* in cases of hepatic cirrhosis, the liver generally shows obvious signs of enlargement; the effusion is in these cases probably as often induced by a non-suppurative perisplenitis as by a peritonitis localised about the liver. It would be well also to mention cardiac weakness from any cause as a possible reason for the occurrence of ascites only partially due to cirrhosis of the liver. If the cardiac weakness were to be recovered from or temporarily improved by treatment, the ascites might, at all events temporarily, be got rid of. Like the author and some others, I am inclined to think that the method of operative interference is only likely to give good results when the liver is enlarged, or at any rate, as far as clinical examination can determine, not decidedly small. In many of these cases an equally good result would be obtained by a few tappings, sometimes followed by the application of pressure to the abdomen, as recommended by Dr. Alexander Morison.

[1] Medical Society's 'Transactions,' 1900, vol. xxiii, p. 70.

Dr. HALE WHITE.—The author has referred to a paper which I published nearly ten years ago, and it is interesting to me to hear that his later cases support the contention I then urged. I may say at once that the cases I have seen since confirm the belief I then expressed, that the onset of the ascites in uncomplicated cases of cirrhosis of the liver is of very bad augury. After all, that is the classic opinion held by Watson, Niemeyer, Fagge, and others. I think the reason why the attempt has been made to deal surgically with ascites due to cirrhosis of the liver is because those who have made it have not thought sufficiently about the pathology of the disease. Seeing the liver cirrhosed, they have jumped to the conclusion that the cirrhosis was due to the pressure of the fibrous tissue on the radicles of the portal vein; but I think that is not so,—in fact, that this has really very little to do with it. We know, for example, that pressure upon veins alone will not lead to effusion and œdema. A man may have a large aneurysm pressing upon a vein without any œdema. Starling and others have ligatured the portal vein in dogs without any production of ascites. I take it that a man with cirrhosis is like a man with granular kidney. He has a gradually increasing amount of fibrous tissue in his liver, but that is only part of a general disease of which we understand very little. In both cases the onset of ascites is liable to occur, and we cannot foretell when it is likely to occur. The man with hepatic cirrhosis is peculiarly liable to ascites, which is usually fatal in two months. Another symptom of great importance, as showing that the cirrhosis of the liver is really a general disease, is the swelling of the feet. I have paid considerable attention to that point, and many patients, I have noticed, have complained of swelling of the feet before any ascites, therefore the fluid in the abdomen is not the cause of the swelling of the feet. Nor can the pressure of the liver be the cause, because it may be of normal weight and size, and yet the swelling may occur. If it were due to pressure upon the vena cava we should expect a large flow of blood in the superficial veins, which is not the case. I think that ascites in an uncomplicated case of cirrhosis should be regarded as an expression of the severity of a general disease, and not as a local symptom. Further, it should be looked upon as the beginning of the end. Then we should hear less of the attempts to treat it by operation. When ascites can be successfully treated by operation it will be found that the ascites is due not to the cirrhosis, but that there is some peritonitis, to which, and not to the operation, the cure is due. I may mention as further evidence of this that I took at random all the cases of ascites which came into the post-mortem room, and I discovered that a very large number of these

patients were unaware that they had the disease at all. A man, apparently perfectly healthy, may break his neck and be brought to the hospital, and he turns out to have cirrhosis of the liver. A large number of the people who have cirrhosis of the liver present no sign of it during life. That is on all-fours with what we know of granular kidney, for many of these subjects have shown no symptom during life. With regard to laparotomy one case struck me very much as showing that the ascites in these cases is not due to pressure upon the portal vein, for although there was much cirrhosis of the liver seen at the operation there was no evidence of pressure upon the portal vein as shown by distension of any of its radicles.

Dr. Thomson.—I agree with the last speaker as to the importance of swelling of the feet, and also that it may sometimes be an early diagnostic symptom of cirrhosis.

DISCUSSION ON IMMUNITY

On March 12th, 1901

OPENED BY

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Although some observers may have modified their opinions during the past eight years as to the exact part played by Metchnikoff's phagocytes, all will agree that without his epoch-marking work it would have been impossible to discuss other theories with any degree of intelligence, for upon cell reaction the "side-chain" theory of immunity and antitoxin production depends for its inception and conception. Whilst in Edinburgh Dr. Cartwright Wood and I carried out a series of experiments on the production of immunity by means of soluble products, in which we thought we obtained a condition in which special activities of the cell—comparing the cell to a many-faceted body, each facet of which was enabled to withstand the attacks of poisons or substances which they had been trained to resist—were drawn out.

Cartwright Wood had already pointed out, in his paper on 'Separable Enzymes,' that the poisons of micro-organisms might be looked upon as "separable functions" or substances having the power of carrying on

the functions of the cell, which could overflow and pass into solution and act outside the cell. Bouchard had suggested that not only connective-tissue cells but other cells of the body are constantly secreting substances which have the power of neutralising the toxic waste products of the body, though it was left to Behring to demonstrate that the introduction of certain toxic substances into the blood is rapidly followed by the appearance in the blood of substances which have the power of neutralising the antitoxins.

As to the "overflowing" of antitoxins from the cells, it is maintained that this is comparable to the overflowing of the toxins from the bodies of organisms. There are some "properties" or "functions" which appear to be separable only with great difficulty from the bodies of micro-organisms; so, also, there may be certain properties or functions which are more intimately bound up in the protoplasm of the cell. In so far as these are distinct I maintain that immunity is distinct from antitoxin production, but, in so far as they are interchangeable and collateral, immunity and antitoxin production must run side by side. With regard to Bütschli's theory of the structure of protoplasm and the relation of metabolic products to the protoplasm, I may point out that, if we accept this theory, then immunity and antitoxin formation, though not the same, must in many cases be very nearly related.

Although various theories have been advanced as to the mode of production of these antibodies, there is now a general consensus of opinion that they are the result of a special stimulation of cells, especially of the connective-tissue cells, by special toxins, and that there is an extraordinary development of the special resisting function of the cell which may go on to such an extent that the antibody overflows into the fluids in which the cell was bathed, just as the special toxins and enzymes overflow into the fluids around the toxin-producing bacteria, or the enzyme-producing yeasts. There now seems to be

nothing extraordinary in this, except as regards the specific interaction, for, as Bütschli and his school have pointed out, we must look upon these special substances as being formed by the cells, and as in some cases remaining in a loose form of combination, but in others thrown out beyond the bounds of the protoplasm itself; whether the toxin be in the organism itself or outside, and whether the antitoxin be within the resisting cells or outside their protoplasm, the antibodies appear to act and react, one upon the other, very directly.

At this point it was naturally suggested by workers in this field—Fischer, Weigert, and Ehrlich especially—that, as so many different antitoxins could be formed in response to the stimulation of the different toxins, there must be some very special affinity between the specific toxin, say, and certain special cells, or even special parts of the protoplasm of these cells. Ehrlich insists that it is only when a substance can be taken into or bound to the cell, and combined with some element in that cell, that any immunity against pathogenetic substances can be gained by the cell. This is a most interesting statement, as its acceptance involves the theory that a toxin must be assimilated by the cell before an antitoxin can be produced; consequently, the whole question of antitoxin production must be closely bound up with the processes of nutrition. As the result of the assimilation of the proteid toxin we have the production and overflow of antitoxic substances from the specially stimulated cell, but the production of immunity against disease or the secretion of antitoxin appears to be only a side issue, as it were, or rather part of a general process going on where albuminoid substances are being assimilated by living protoplasmic cells. Ehrlich maintains that "from the standpoint of immunity the toxic action of a toxin is a matter of accident, indeed of indifference, since a toxin does not produce its antitoxin by virtue of its toxic power, but because, being introduced into the animal body in such a way that its immediate destruction is avoided, it is

assimilated." To put it more bluntly, the cells of our body are able to acquire immunity against organic toxic substances only because they are capable, in the process of nutrition, of taking these proteid toxic bodies into combination. Indeed, it has been demonstrated by Myers, Ehrlich, and others, that specific proteid substances obtained from different sources are, if introduced into the body in such a manner that they are not broken up or destroyed, capable of producing in the serum of the animal certain antibodies. One of Myers' experiments will serve as an example; he introduced crystallised egg albumen into the peritoneal cavity of a rabbit. After this had been repeated weekly for a period of some six or eight weeks, a small quantity of the blood of the rabbit was taken, and the serum separated from this was added to a solution of the original crystallised egg albumen. This addition resulted in the combination of the two substances, and in the precipitation of the egg albumen, and such quantities of each may be added that every particle enters into combination, the albumen and its antibody neutralising one another completely and exactly, in this way acting just as do the proteid toxin of the diphtheria bacillus and its antitoxin. If the albumen used in such an experiment be pure, its range of activity appears to be exceedingly limited, whilst if it be a "mixed" albumen it appears to react against a correspondingly large number of albumens. We have here an analogous condition to that found in connection with toxins and antitoxins—perhaps comparatively simple and specific bodies; and bacterial products and antibacterial products —much more complicated substances. The proteid poisons of diphtheria, however, are not pure toxic substances; indeed, the toxic factor appears to be of less importance than some other portions of the molecule that give rise to the special stimulation producing antitoxin, and it soon became evident that proteid poisons may become so far modified as regards minor groups of molecules (the main combining molecules remaining the

same), that cells may be brought to assimilate or combine with these molecules in such a fashion that they form within their protoplasm substances which, either in the cell or separated from it, can combine with the whole molecules and, along with them, with the secondary and smaller molecules to which the special toxicity may be attributed, and thus neutralise them.

That something of this kind may take place, Ehrlich points out, in connection with the neutralising power of antitoxins, as antitoxins neutralised not only true toxins, but also what he calls toxoids, *i. e.* substances apparently formed from toxins, having many of the properties of the toxins but retaining little if any of their lethal activity. He proved this in connection with diphtheria toxins by testing the combining power of an active toxin, and then, after keeping this toxin in a warm chamber for some time, again testing both its lethal and combining powers. Its combining power with antitoxin remained the same, but its lethal power had fallen enormously, to one half or one third of its original strength. Having determined this, he found that in the case of tetanus toxin he could diminish its activity by adding bisulphide of carbon. He found, however, that this innocuous toxoid still retained its remarkable immunising and antitoxin-producing constituent.

These toxic proteid molecules may be either toxic molecules linked to the proteid molecule, or a proteid molecule in which certain replacements have taken place. In any case, they appear to be easily linked to the living cell, and to be able to stimulate it to produce antitoxin. They are always formed in larger quantities where albumens are already present than when the proteid molecule has, as it were, to be built up. If now the toxic molecules, produced in these albuminous fluids in such large quantities, can be modified as are the molecules produced in fluids containing less albumen, should it not be possible to obtain large quantities of non-toxic proteid molecules which, assimilated by the

cells, will induce the formation and overflowing of antitoxins, antitoxins capable of neutralising not only the principal toxoid or large molecule, but this same toxoid molecule with its linked-on smaller toxic molecules? Cartwright Wood has proved that this is possible, and we have the result in the rapid production of antitoxin by the injection of serum-toxin, which contains an exceedingly small amount of the active toxic substance, it still retaining its power of stimulating the cells to produce antitoxin. All this has been confirmed by Ritchie. The molecule, able to become assimilated by the cell, still retains its characteristic power of forming "antibodies."

The study of the ferments formed by pathogenetic organisms can perhaps be best advanced by continuing the study of the non-pathogenetic enzymes, hæmolytic substances, and the agglutinins, in connection with which Ehrlich, Pfeiffer, Gruber, Durham, and others, have already obtained such brilliant results.

Bound up with the theories of immunity and the source of antitoxin is the question of the nature of antitoxin. One of the original theories put forward by Roux and Vaillard, and afterwards emphasised by Ehrlich, that antitoxin was the result of the special stimulation of certain cells, receives support from a very large number of observations made during the preparation of antitoxin, especially in the fact that it is only where there is marked reaction, especially of a local character, that there is any increase in the amount of antitoxin produced. I lay marked stress on the local reaction because the toxin injected must exert its greatest stimulating power,—in fact, one may almost say its only stimulating power,—on those tissues with which it comes directly in contact, that is before it becomes mixed with any large quantity of lymph or finds its way into the circulation, in which, at the temperature of the body, the combination of toxin and antitoxin goes on with great rapidity, the amount of antitoxin in the blood of some of the animals under treatment being thousands, and even tens of thousands, of times the

quantity required to neutralise the whole of the toxin injected. Indeed, it will be found that the toxins injected into horses that have been under treatment for some time would, if they made their way directly into the circulation, be neutralised over and over again by the antitoxin which in such animals is present in large quantities and thus be rendered quite incapable of setting up any reaction at all. In the subcutaneous tissues, however, where it can act almost directly upon the connective-tissue cells, its action being only slightly impeded by the small quantity of antitoxin in the lymph of these tissues, it may stimulate them to set up the production of the antibodies in a marked degree; so that under favourable conditions the production of antitoxins can go on for a long period after large quantities of antitoxin have been stored up in the circulating blood. Such an explanation appears to be all the more probable from the fact that the constitutional symptoms are of such short duration, whilst even the local reaction is rapidly neutralised. Without some explanation of this kind, too, it would be exceedingly difficult to understand how it is that the vital organs of an animal are so little affected during the treatment necessary for the production of antitoxin; the amount of antitoxin in the blood is sufficient to protect the whole animal, except those tissues into which a larger amount of toxin can be introduced than can be neutralised by the antitoxin in the blood and lymph in these tissues. It is for this reason that, as the process of treatment goes on and more antitoxin is formed, stronger and stronger toxins are necessary for the production of even a slight local reaction.

Behring has drawn attention to the fact that the tissues may become hypersensitive even when large amounts of antitoxin are present. Such a condition we may expect to find in the more highly organised tissues for which the toxin has a special affinity. Here there may be a kind of local hypersensitiveness induced through want of equilibrium due to over-stimulation. The amount

of antitoxin may be great, quite sufficient to protect against toxins introduced in the ordinary way, but inadequate, because it cannot all act at one place and at the same time, to counteract the local action of poison specially introduced in bulk and at one point.

As regards the amount of antitoxin produced, I may mention that taking the lethal activity of a toxin to represent its quantity and neutralising power I have records of the formation of 20,000 and even 40,000 times as much antitoxin as I use toxin, whilst in no case in which there was any rise at all were there fewer than sixty-three antitoxin units for every unit of toxin injected, and in one horse the lowest figure obtained in any experiment was 5588 antitoxin units per unit of toxin introduced. This is remarkable, and indicates one of two things: (1) most probably that the immunising or antitoxin stimulating substance is of the nature of a toxoid, or of a proteid molecule that is not highly toxic; and (2) that the process of antitoxin formation goes on long after the special and specific stimulus has been removed.

The idea that antitoxin is merely a modified toxin I strongly dissent from. It is now an old story, but I think it may be well to mention that attempts were at one time made to prove that an antitoxin might be a simple derivative of a toxin; for example, that it might be produced by the electrolysis of toxin. It was soon found, however, that in this case there was merely a destruction of the toxin by the chlorohypochlorites produced when a weak saline solution is electrolysed, for, when no sodium chloride is added to the solution of toxin to be thus treated, there is comparatively little destruction of toxin. Later, Professor T. R. Fraser, as the result of his observations on snake venom and antivenin, came to the conclusion that antivenin was a modified venom and that the antitoxin or immunising substances produced, originate, not from vital reactions of the cells of the body to the toxins, but from chemical changes

in toxins themselves, the toxins being disintegrated, and the antibodies, which, according to this theory, are amongst the normal constituents of the toxin, being left unaltered, or, at any rate, but slightly altered after the removal of the purely toxic molecule, and capable of again combining with fresh toxic molecules presented to them. In the horse, however, the amount of antitoxin formed is out of all proportion to the amount of toxin introduced, in some cases being hundreds of times as great, even calculating the test dose of toxin at its lowest toxic value of one instead of a hundred. When it was found, however, that toxins become converted into toxoids outside the body, Fraser's theory was apparently more tenable, as it was naturally suggested that these toxoids might be transition stages between toxin and antitoxin. Against this, however, are the following facts:—The toxoids, like the toxins, have the power of stimulating the cells to produce antitoxins, but they have the power also of acting like toxins in neutralising antitoxins. Again, Sidney Martin and Cartwright Wood, in the preparation of their albumoses, obtained toxins of an exceedingly active character by growing the diphtheria bacilli in a fluid containing albumen. A kind of external metabolism then appears to take place; an enzyme is formed by the bacilli, and this enzyme apparently is capable of acting upon the albumens so as to produce "albumoses." When this mixture of albumen, albumose, and toxin is heated to 60° C. it so far loses its toxic activity that although, before heating, a twentieth or a fortieth or even a smaller fraction of a c.c. is sufficient to kill a guinea-pig, three or even five c.c. of the heated substance produces no appreciable toxic effect when injected into a guinea-pig, or at most induces a temporary swelling which soon passes off. Although it has lost its toxicity I find that *it exerts absolutely no antitoxic action*, and is no more capable of neutralising toxin than it was before it was heated, though when introduced into the tissues of the horse, as already stated, it is found to

still possess in a most remarkable degree the power of stimulating cells to the production of antitoxin. It is a toxin greatly modified, no doubt, but not in any way converted into an antitoxin, as it neither increases nor diminishes the antitoxic action of a test dose of antitoxin acting upon a test dose of toxin; it has the physiological action of a toxin from the nutritive point of view—it may be assimilated, and so produce a specific reaction in the cells, but it does not possess the power of combining with, or assisting, either toxin or antitoxin outside the cells.

These albumoses, then, whatever may be their exact character, are not specially toxic, but, on the other hand, they are in no sense of the term antitoxic. They have the power when introduced into the body of setting up the formation of antitoxin, and also the power of producing a very definite immunity. We have also evidence of the cellular origin of antitoxin in the way in which it continues for long periods in the fluids of the animals in which it is produced, long after all trace of toxin has disappeared, although it may be and is thrown out as a foreign body from animals into which it has been injected.

As early as 1893 Roux and Vaillard pointed out that animals treated with toxin might lose blood equal to the whole of the body weight, if this loss be prolonged over a period of several days, without there being any marked falling off of strength in the antitoxic value of the blood that remains. Here we have evidence that the production of antitoxin must be going on as the continued result of a special stimulation of the antitoxin-forming cells; the toxin has all disappeared, but antitoxin is still being formed. Salomonsen and Madsen have also proved that there may be an actual rise of antitoxin after considerable volumes of blood have been withdrawn from an animal treated with toxin, and they agree with those who maintain that there is a new production of antitoxic substance going on as a result of a special stimulation of the

tissues. My own observations all go to prove that an antitoxin is in a great measure formed locally, that it is the result of a special reaction between the toxin and the connective tissues, and that the antitoxin is produced as a kind of secretion from these special cells reacting to the special stimulation.

The discovery of the linking-on of toxin to proteid bodies, and particularly to special proteid bodies, and the assimilation by cells, with the consequent appearance of antibodies, is one of the most remarkable contributions to our knowledge of immunity that has yet been made. In regard to the question of polyvalent sera I may point out how important are Durham's observations in connection with the subject of relapses.

There are several points to be cleared up in connection with the question of specificity. Salomonsen and Madsen, and later Behring, Bulloch, and others, have shown that there is a constant draining away of antitoxin from animals. In animals injected with antitoxin from other species this leakage goes on very rapidly, and it is for this reason that the passive immunity—if one may use the term—conferred by antitoxin is of such short duration, for Behring and Ransom have demonstrated that when the antitoxin is formed in an animal, it remains present for a considerable period; here we have at once an explanation of the fact that a patient injected with antitoxin is protected for a comparatively short period, whilst a patient who has suffered from an attack—even of diphtheria, in which the period of protection is not nearly so prolonged as in other diseases—is protected for a considerably longer period. In this must be sought the explanation of the fact that we meet with relapses somewhat more frequently in cases of diphtheria treated by injection with antitoxin, the antitoxin injected coming from a species—the horse—different from the patient injected.

The question of specificity, however, is much more fundamental and far-reaching even than this. For Cart-

wright Wood, in a series of experiments carried out during the last four or five years, has shown that in the rapid method of production of antitoxins it is necessary to use in the preparation of the serum toxin a serum taken from the same species of animal as that which is to be injected. He has found, for instance, that the serum toxin prepared with the serum of a horse gives admirable results when injected into a horse; but Ehrlich, using the same batch of serum and injecting a goat, found that he obtained practically no positive results; and Wood, carrying on his experiments with rabbits, guinea-pigs, and pigeons, found that the specificity was in each case more or less distinctly marked, and that each animal could only be treated satisfactorily—*i. e.* with the formation of antitoxin in large quantities or the production of a definite immunity—when the serum toxin is prepared with the serum of the animal to be injected. This points rather to the fact that the intermediate link described by Ehrlich is a most important factor in the production of immunity, the proteids contained in these albumoses being more readily assimilated by the cells, when cells and proteid are both, as it were, of the same species. The blood of one species, then, may be looked upon as behaving as a foreign body when introduced into another species.

This, again, has a most important bearing on the question of assimilation, and it may be that the toxin or toxoid is simply linked on to another or intermediate molecule which keeps it in contact with the cell protoplasm, and so enables it to set up the production of antitoxin.

Whether we are justified in accepting Durham's theory of specific reaction, or that put forward by Cartwright Wood, we are gradually working out the extreme specificity of immunity in most forms of disease. A *general* insusceptibility there is in many cases, and this may usually be increased, but it may also be diminished in certain cases where a marked protection against *specific* bacteria and bacterial poisons is obtained.

DISCUSSION.

Prof. A. E. Wright.—I do not think with Prof. Woodhead that the theories of immunity which are propounded by Metchnikoff and Ehrlich respectively can be regarded as theories which merge into each other. Metchnikoff's phagocytosis theory is designed to explain the bactericidal effects observed in the organism. An explanation is found for these in the assumption that the organism of the higher animals corresponds to a colonial aggregation of monocellular organisms, some of which in the form of white blood-corpuscles still possess the properties and exercise the functions of the original free-living monocellular organisms. There is no doubt that the fact that white blood-corpuscles emigrate towards the seat of a bacterial invasion, and that the bacteria are afterwards found in the interior of the white blood-corpuscles, and often in a condition of disintegration, is brought much nearer to the understanding by the theory propounded by Metchnikoff that the bacteria are incorporated and digested by phagocytes. On the other hand, when we turn from the consideration of the inflammatory and bactericidal effects seen in the organism to the consideration of the problem of antitoxin formation in the organism, the theory of immunity propounded by Metchnikoff fails entirely to provide anything in the way of an acceptable explanation. Metchnikoff's view that the white blood-corpuscles void antitoxins into the body fluids under the stimulus of a toxin may, it is true, be crudely compared with the ex-voiding of mucus which takes place when a snail is brought into contact with alcohol, the toxin of the yeast plant; but the mental picture will not explain to us the fact that a number of different specific antitoxins are produced in the organism in response to the introduction of a series of different toxins. This last, as distinguished from the problem of the bactericidal effects exerted by the organism, is the problem that Ehrlich has set himself to solve. He asked himself not how it was that bacteria were destroyed in the body, but how it was that when a guinea-pig was injected with a poisonous element—and in some cases the poisons in question were poisons which were brought in contact with the responding guinea-pig for the first time in the history of the individual and the race—an antitoxin was produced whose chemical properties fitted those of the poison as accurately as a key fits into its corresponding lock. Professor Ehrlich has drawn attention to the fact that such antitoxin production takes place only when the poisons which are injected are albuminous substances or substances allied to them—when, in other words, the poisons

are such as may, I think, be conveniently denoted as "poisonous foodstuffs." Such "poisonous foodstuffs" will be taken up into cells by virtue of the fact that there are in the cells molecular groups—side-chains—which possess chemical affinities for the substances in question. Following upon this "occupation" of the side-chains by the poisonous foodstuffs there will occur, in the opinion of Ehrlich, a re-formation of similar side-chains in the cell, which will gradually transform itself into a process of "internal secretion," the product of secretion being a substance identical in its chemical affinity with the toxin with the original "side-chain" constituent of the cellular protoplasm. The further question as to what kind of cells contain side-chains which can be thrown off as antitoxins has been somewhat incompletely treated by Ehrlich; for while he has emphasised the fact that the cells whose side-chains are affected by the toxin are those which respond with a formation of antitoxin, he has, through a certain want of preciseness in the setting forth of his theory, allowed it to be understood that the response takes place only in the group of cells which the clinician recognises to be affected by the poison. Such will be the case only with "monotropic" poisons—*i. e.* poisons which affect only one variety of cell. In the case of "polytropic" poisons—and a very large number of poisons must come under this category—the chief response—*i. e.* the chief antitoxin production—may take place in tissues which the clinician cannot discover to have been affected. Under this category will come the white blood-corpuscles, which when affected by the toxin will naturally be involved in the production of antitoxins. It is, in my opinion, only in this respect, and even here only incompletely, that the theory of Metchnikoff conforms with Ehrlich's theory of the production of antitoxins. I now pass to consider the possibility of applying the theory which Ehrlich has propounded to explain the production of antitoxin in the system, to the explanation of the production of bactericidal substances in the blood. A comparison cannot be established between the two processes when it is considered that the constituents of the bacterial protoplasm are in many cases poisonous, and that these constituents pass into solution in the lymph when bacterial cultures are injected into the subcutaneous tissue. An analogy is thus immediately established between the injection of toxins and the injection of bacteria. Similarly an analogy emerges between the response in the form of an antitoxin formation which takes place after the injection of a bacterial toxin and the response in the form of a production of anti-bacterial substance which has, in the case of cholera and typhoid fever, been observed by myself to take place in the case of bacterial injections. Ac-

cording to these the essential difference between an anti-bacterial substance and an "antitoxin" (using the term in its ordinary sense) will be that the substance produced in the latter case has a chemical affinity for the substances contained in bacterial filtrate, while the substance found in the former case has an affinity for a substance which is a constituent of the bacterial protoplasm. When it is considered that all substances—not being foodstuffs—which have a chemical affinity for a component of the living protoplasm are by definition poisons for that protoplasm, the circumstance that an antitoxin to a constituent of the bacterial protoplasm is capable of functioning as a bacterial poison is easily explained. Taking my stand upon the identification of anti-bacterial substances with antitoxins (using the term in its widest sense), I may point out that the phenomena which come under observation after an injection of toxin come under observation also after an injection of bacteria. Just as in the first case the injected toxin circulates for a time in the blood of the injected animal, so after the injection of bacteria a similar negative phase probably occurs. It occurs, so far as my observations have gone, in the blood after an anti-typhoid inoculation, the negative phase being marked by a decline in the normal bactericidal power of the blood. Again, just as in the case of an animal which has been treated with an excess of toxin, the blood may—*e. g.* in the case of animals injected with excessive doses of snake venom—contain toxic in lieu of antitoxic elements at the period when the blood is usually drawn off, so apparently, in the case of an animal injected with an excess of a bacterial culture, the blood may, when drawn off, contain substances which are not bactericidal but anti-bactericidal. Such substances I have recently described [1] as having been found in the specimens of "anti-typhoid sera," which are placed on the market for therapeutic use. Apart from an actual demonstration of the presence of such anti-bactericidal substances, I have concluded the presence of such substances in "therapeutic sera," from the phenomena which I have observed in connection with a sample of anti-plague serum which has been prepared by Dr. Galeotti in Bombay, in the case of certain anti-streptococcic sera, and in the case of a sample of anti-Malta fever serum prepared by myself. In the former case, where I studied the effects of the anti-plague serum in question in association with my colleagues of the Indian Plague Commission, the serum, though when given by itself did not exert any noticeable toxic symptoms in guinea-pigs, had the effect of hastening death in guinea-pigs who were at the same time inoculated with plague.

Professor SIDNEY MARTIN.—There is one thing in the question

[1] 'The Lancet,' Jan. 12th, 1901.

of immunity which is of extreme interest, viz. the subject of the specificity of proteid matter is now being verified. In a paper which I read before the Royal Society on the toxic substances in *Abrus precatorius* some years ago I described two toxic proteid substances, and the criticism then made was that it was not conceivable that a proteid should be poisonous, and that there must be a *tertium quid* added to the proteid substance. The same feeling prevailed when papers were read before that Society on snake venom, viz. that it was difficult to believe that a proteid could be poisonous or could exert any toxic action upon the body. That idea is now exploded, and it is admitted that there is no reason why a substance having the constitution of a proteid should not exert deleterious influence upon protoplasm. The question is a very difficult and delicate one, but a cell may reject certain substances and take in certain others for which it has a chemical affinity. This affinity of special substances for cells has been brought out most clearly in the work done of late years in regard to the effect of toxins upon the body, and of antitoxins, and is, indeed, one of the most interesting aspects of artificial immunity.

Dr. RITCHIE (Oxford).—The advances which have been made in the recognition of the fact that organic substances can actually form materials poisonous towards the body are of great importance. Still more interesting is the fact that, as this field of research is being explored, we are more and more bringing what was rather a particular aspect of pathology into line with general biology, and thus proving that the fundamental conceptions of biology and pathology are the same. In this connection I agree with Professor Woodhead as to the importance of the work which was done by Dr. Myers, whose death we all deplore. His investigations linked the question of immunity with processes which may go on normally in the body, and incidentally disclosed a method of distinguishing closely allied bodies, such as albumens derived from different sources—a method more delicate than any hitherto available. He, in fact, raised the very important question of the specificity of the albumens of a given animal. With regard to the points in which I am more particularly interested in this connection, one is the enormous want of proportion which may exist between the amount of toxin injected in the process of immunisation against tetanus and the amount of immunity which one may obtain. In using the toxoids to which Professor Woodhead has alluded, and which were made by the action of hydrochloric acid on the crude toxin, I immunised animals, or rather series of animals, not, as is usually done, by successively increasing doses of toxin, but by using the same doses on each occasion, and these relatively small; and in this way some very interesting results

came out. One is that I have alluded to, namely, that the amount of immunity produced, reckoned in minimal lethal doses, is very much greater than the amount of toxin producing it, the latter being also reckoned in the same way. In this connection one must carefully distinguish, in talking of the immunity of an animal against a particular poison, between the capacity which the animal has of resisting that poison, and the capacity which it has of producing an antitoxin which may neutralise the poison in the body of another animal. These are two things which bear no essential proportion to each other. Thus I found that in an immunisation produced by four doses of toxoid, which as toxin had contained 40 M.L.D., a resistance against about 100 M.L.D. was produced, but the serum of such an animal contained only enough antitoxin to neutralise about 2 M.L.D. By continuing the immunisation process with four other doses, and thus giving toxoid, which as toxin contained in all 80 M L.D., an enormous rise in the resistance took place, an animal thus treated withstanding 600 M.L.D. Its serum would now contain enough antitoxin to neutralise 75 M.L.D. Therefore in the rise of immunity the first thing which happens is a great development of resistance at a time when there is very little antitoxic power in the serum. This appears to be a very important observation from the standpoint of the theoretical considerations that have been brought forward to-night. I must say I am with Professor Wright in so far that I do not think it is possible to harmonise the systems of Metchnikoff and Ehrlich. Metchnikoff's latest position is very difficult to make out, but so far as one can gather it is far removed from Ehrlich's. Ehrlich's theory has essentially to do with the metabolism of cells, and the results I have obtained so far agree with the idea that antitoxin production against such a disease as tetanus is of the nature of over-regeneration. There is one statement which has been made to-night which is, I think, incorrect. It is not the case that Ehrlich attributes the production of antitoxin to the brain cells alone. With regard to certain animals he does make such a statement, but he quite recognises that in other animals there may be cells in other parts of the body which have affinities for tetanus toxin just as the brain cells have, and which may therefore, like the latter, be the seats of the formation of antitoxin. There is one other point which I should like to mention, which has always appeared to me difficult of explanation, namely, why immunity, when once produced in an animal, should go on increasing. It is odd that in an animal with an enormous amount of antitoxin in its serum, the injection of fresh toxin should not result in the neutralisation of the latter before it can have any effect on the fixed cells of the body. The explanation usually given, that toxin and antitoxin only

combine slowly, does not appear to me to wholly meet the known facts. It may be that just as in such diseases as typhoid, cholera, etc., where two bodies are at work, so there may be some linking body present also in such apparently simple cases as tetanus and diphtheria.

Mr. T. J. Bokenham.—The only point to which I wish to draw attention is in regard to the functions of the liver in protecting against infection by the colon bacillus. If you inject a culture into the blood of a rabbit, in a very short time no free microbes are to be found in the blood; but if you examine the liver you will find large quantities of bacilli collected in and around the liver cells. If you take a virulent culture of the same, the first examination of the blood will give a result comparable to that obtained by the non-virulent culture, but within half an hour the cultures made from the blood at that period begin to give positive results, so that although there are no bacilli circulating after a few minutes they get back into the blood after a short time, and the animal ultimately dies of septic infection and the liver is found to be full of bacilli. If you inject this virulent culture into an animal which has been first of all protected by the colon serum, then one obtains a result exactly comparable to that of the weak culture.

Mr. Plimmer.—It is a very good thing that this subject has been brought forward and discussed here, as diffusion of knowledge of the subject may prevent some of the absurd errors attending the use of antitoxin which one sees recorded in the medical papers,—as, for instance, the case of the man who injected for the cure of aneurism three different kinds of antitoxic sera. With regard to natural immunity, I was working last summer in Italy in a malarial region, and I met with certain cases of natural immunity to malaria. Nine such cases I saw myself, the ages of the subjects varying from eighteen to fifty. All of these people had lived in this district all their lives. Two of them allowed themselves to be bitten by *Anopheles*, very rich in malaria parasites, without any result at all. Celli also records a number of cases of the kind. There is no sufficient reason for their immunity, because there is here no question of an antitoxin. With regard to Mr. Bokenham's statements as to the colon bacillus, it is well known that any bacillus injected into the veins will disappear from the circulating blood in from five to seven minutes, even the anthrax bacillus, and they can be found in the leucocytes, which disappear with them in the organs, especially spleen and liver, and in the endothelial cells of these organs.

Dr. W. Hunter.—The question of the cells concerned in producing this antitoxin or special products several speakers have touched upon,—the question whether the products are

formed by the cells of the body as a whole, or by cells of a special kind. I have always had a special regard for Metchnikoff's view, inasmuch as the essence of his teaching in regard to immunity is that a special class of cells are concerned in its production, leucocytes and the like. My own observations confirm that view in regard to immunity with reference to one of the changes produced in the blood by toxic products, viz. that of hæmolysis. The general teaching with regard to this hæmolysis is that these bodies acted upon the corpuscles, destroying them and liberating their hæmoglobin. I found with regard to one of the most powerful that it produces hæmoglobinæmia, but the most interesting fact came out, that if I excised the spleen that body produces no effect on the blood at all. This fact is one which I always considered to possess great importance, though I do not know whether it has received attention in this relation. The whole tendency of this work, just as with regard to hæmolysis in connection with immunity, is of far too mechanical a nature. It is a pure test-tube affair. The final result of all experiments which I have carried out with regard to the nature of hæmolysis was to reduce the matter to the action of certain cells, and not merely of cells of the body generally, but cells of the mesoblastic type in the intestinal tract and the spleen; and the hæmolysis is induced by products possessing a globulicidal action.

Dr. Rose Bradford.—It is well known that acquired immunity hitherto has not been observed in reference to diseases produced by animal organisms, especially protozoa, but instances have been quoted of natural immunity to malaria. Now there are other diseases associated with protozoa in animals, in which natural immunity has been observed, but so far as I know there is only one instance of acquired immunity to the effects of protozoa. There is a disease in America and the Cape called Texas fever, or red-water, dependent upon the presence of an amœboid organism in the red blood-corpuscle. It is well known that in Africa, where there are so-called salted animals which are immune to this disease; and it has also been shown by Dr. Eddington that an acquired immunity can be produced by a certain method of inoculation, that is, by taking the blood of salted animals and transferring it to other animals. Apart, however, from this instance it appears that immunity has not hitherto been produced in diseases associated with the presence of protozoa or fungi.

Professor Macfadyean.—What has just fallen from Dr. Bradford rather suggests that in this as in many other discussions it would be well to begin with a series of definitions. I am not sure that it would not be useful to attempt to define what one means by immunity. The necessity for this I may

illustrate by adding a little to the information which Dr. Bradford has just given. It is true that there does exist a disease known as Texas fever, which is caused by a microscopic organism assigned to the animal kingdom. It is also true that there are large tracts of country, both in the United States and in Africa, where the native cattle exhibit a remarkable degree of immunity, *i. e.* they do not die from this disease, and do not exhibit any symptoms of impaired health; but it is a very peculiar sort of immunity, because experiments have shown that these apparently healthy animals, without exception, harbour the parasite in their blood. That is a form of immunity which is extremely difficult to fit in with any theories yet broached. The parasite itself does not appear to be in any sense attenuated, for the blood will often set up a very virulent attack of the disease in an animal from outside the area. There is one other similar fact, viz. that in some of the small ruminants, what may pass for absolute immunity for the organism of cattle plague may be present. It is not an immunity in the ordinary sense which makes it impossible for the bacteria to propagate in the body, for it can be shown that the blood of some of these ruminants is virulent when tested by inoculation.

Dr. Sims Woodhead.—In malaria we have a condition very similar to the two instances last mentioned, for the malarial parasite, in large numbers, has been found present in the blood of children who appeared perfectly healthy. I believe it is now held by many people that the "adiment" is really derived from broken-down leucocytes. If you take old serum it does not act, but if you take recent serum you get a well-marked effect. With regard to the relation of immunity and antitoxin production, I believe that although these often go on side by side they are not identical. It is possible to produce in a horse a condition of immunity at a late stage of antitoxin production, when it is no longer possible to obtain any antitoxin; but conversely you can obtain antitoxin of high potency in animals which, according to Behring, are even less immune than usual, and where certainly it may be not very high. As to Professor Wright's point, viz. the disappearance of the anti-bactericidal power of the blood, especially that observed in connection with typhoid fever, I believe it is a fact that you may get an immunity against certain bodies developed in certain directions, but as this is achieved there is a very marked interference with the bactericidal power of the blood in other directions,—in other words, you divert so much of the activity in one direction that it may be entirely lost in another. Then as regards the special activity of toxin upon the special tissues. There is no doubt that toxin does affect the nervous system of the guinea-pig in a

much more marked fashion than it does that of the rabbit, a fact which has been established by Roux and others. I may point out in conclusion that, after all, it is in great measure due to Metchnikoff's work on this subject, followed up by that done by Behring and Ehrlich, that such a discussion as this is possible.

SUGGESTIONS FOR A POSSIBLE IMPROVEMENT

IN THE

METHOD OF REMOVING STONES AND MORBID GROWTHS

FROM THE

INTERIOR OF THE BLADDER.

BY

SIR THOMAS SMITH, F.R.C.S.

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THE object of this paper is to call attention to a possible means of diminishing the mortality of operations which involve the opening of the bladder, whether for the removal of calculi or morbid growths, and this by a considerable modification in the method usually adopted in performing the supra-pubic operation.

Supra-pubic cystotomy is so easy of execution, and so free from the immediate risks of hæmorrhage, shock, or injury to important structures, that it has rapidly gained adherents as a means of removing stones, especially from among those who have had little or no experience in litholapaxy, and have seldom or never removed stones from the bladder by the old operation of lateral lithotomy.

The lateral operation, even in past times, was in the case of children a very successful operation, and attended by a very small mortality when undertaken by competent hands,[1] and it is probable that it would be attended with even less risk in the present day under improved methods of wound treatment.

Supra-pubic lithotomy is by no means free from risk, and there is good reason to believe that the mortality in children operated on by this method is greater than was formerly the case when lateral lithotomy was the routine treatment.

The defects and drawbacks to success in the supra-pubic method are largely due to the open wound which remains after the operation, a wound not easy to drain, and in most cases quite impossible to keep aseptic, and which often necessitates a lengthy and irksome convalescence.

Though now and then the immediate closure of the bladder wound is a success, yet this proceeding always involves some risk; more often the attempt is a failure, and sometimes a disastrous one.

The muscular coat of the bladder, when uncovered by peritoneum, does not lend itself to immediate union by suture; in fact, it rarely unites. In strong contrast to this is the behaviour of bladder wounds united by suture in parts of that organ covered by peritoneum; such wounds where the opposed surfaces are peritoneal readily unite. I take it this fact is undisputed; and the question I wish to raise is whether advantage may be taken of this to improve our present method of performing supra-pubic cystotomy, having in view the circumstances and condition of abdominal surgery at the present day.

This question was frequently the subject of discussion with my late lamented colleague Morrant Baker, and though at that time the development of peritoneal surgery was incomplete, and the comparative safety of opening

[1] See Mr. Morgan's paper on this subject, 'Med.-Chir. Trans.,' vol. lxxiv.

the peritoneal cavity had not been proved by experience, we hoped that if ever it became a comparatively safe proceeding to open the peritoneal cavity, this might afford the best route to follow in supra-pubic cystotomy.

I venture to think that the time has now come when the method of operating in supra-pubic cystotomy might at least be reviewed. The advance and perfecting of antiseptic surgery has diminished so considerably the danger of interference with abdominal viscera, that it may be that the risk is now at an irreducible minimum; at all events, with proper precautions and in practised hands the risk is very small.

The suggestion I have to make as worthy of the attention of surgeons is that in supra-pubic cystotomy, when it is desirable to obtain an immediate closure of the bladder wound, the bladder should be opened through the peritoneal cavity at a part above the site usually chosen, and where it has a peritoneal covering, the wound being immediately closed by suture.

The material used for suture might be subject to the preferences of individual surgeons, being of less importance than the method of its application, which in any case should secure the close apposition of peritoneal surfaces on either side of the wound, and should not penetrate to the interior of the bladder.

In the performance of the operation certain precautions would have to be adopted suited to the requirements of an intra-peritoneal operation, and certain modifications in the routine method of performing supra-pubic cystotomy.

I have to suggest that should an operation such as is under consideration be attempted, the bladder, having been thoroughly cleansed with warm boric lotion, should be completely drained of all fluid, should be very moderately distended with air, and not with fluid; that the wound above the pubes should be somewhat higher than is usual; that the bladder should be opened from within the peritoneum, the surrounding parts being protected by sponge packing; and that the vesical wound should be

closed and treated as after operations for traumatic rupture.

It might be worth consideration whether for this or, indeed, for other operations on the bladder of this kind, Trendelenburg's position would not be more convenient than that usually adopted.

In offering the foregoing remarks to your consideration, I may venture to state that the suggestion therein contained has been held in reserve until the comparative safety of peritoneal surgery has been so far established as to seem to justify the submission of the subject to the criticism of this Society.

DISCUSSION.

Mr. CLEMENT LUCAS.—It occurs to me that the value of this paper would have been increased had a few cases been included in which the operation had been actually carried out. The author's suggestion, if I understand it aright, is that the operation of supra-pubic lithotomy is not at the present time in its most complete state, or as valuable as he would like to make it, and that it would be improved by cutting through the peritoneum. I may point out that supra-pubic lithotomy as at present performed is quite different from what it was when revived by Thompson some years ago. It was then suggested that the bladder should be drained always over the pubes, and that the opening in the bladder should be torn, and not cut. Personally I should never think of tearing open the bladder or of draining it as a routine practice from above the pubes. The best practice doubtless is to disinfect the bladder thoroughly beforehand, and to use a clean cut, and then suture the bladder wound. I do not, however, see clearly what advantage would accrue from the author's suggestion to open it through the peritoneum. Supposing you failed to get adhesions after the supra-pubic incision, then you might get septic infection from the bladder if it were in a bad state. Under such circumstances, to make the opening through the peritoneum would only add an additional danger rather than add to the safety of the operation. Still, if I remember aright, the operation for removal of a kidney was originally advocated in this same way by the same surgeon, and I would therefore suggest that his proposal merits due consideration.

Mr. BRUCE CLARK.—The operation is one which we are generally called upon to perform in a septic bladder. If it were usually or even often performed on an aseptic bladder, the operation would be a very different one, and we might expect to get rapid repair of wounds and so ensure its success; but it is very different when we operate for a case of tumour of the bladder, or enlarged prostate, or a large stone, a sacculated bladder, etc. Under these circumstances, in over 90 per cent. of the cases the bladder is septic to start with, and I should want a good deal of urging before I consented to open the bladder through the peritoneum, thus running the risk of draining septic urine into the peritoneal cavity. Of course if one were driven to do this I daresay a drain might be placed in the peritoneal cavity, so as to ensure the exit of urine and pus, if they found their way into the peritoneum after the bladder had

been sutured, and thus a comparative degree of safety might be ensured; but it is difficult to conceive the circumstances under which one would be justified in deliberately performing such an operation from choice, when a safe alternative was presented.

Mr. FREYER.—The author has not put forward this suggestion in any dogmatic spirit, but for discussion and criticism, and his paper gives us the opportunity of reopening the question of supra-pubic lithotomy. He points out that the operation is a very simple one; but I venture to say that in its ease and simplicity lies its chief danger, as offering a field of experiment to the inexperienced surgeon. It can be performed almost with the instruments in one's pocket case; but we are not to judge of an operation by its ease and simplicity, but by the mortality attending it. I venture to say that the mortality from supra-pubic lithotomy at the present time is simply ghastly. This is rather a strong expression, and I would not use it were I not supported in doing so by statistics. These may be found in a paper written for the 'British Medical Journal' by Mr. Gilbert Barling, of Birmingham, and published in May, 1895. He went to the trouble of getting statistics from various large hospitals in London and the provinces, and he found that amongst some 180 cases of stone reported from six large London hospitals, with medical schools attached, and six large hospitals in the provinces, the mortality from the supra-pubic operation was about 20 per cent., that from lateral lithotomy 5 per cent., and that from litholapaxy about the same. How, sir, in face of these statistics, surgeons can go on performing supra-pubic lithotomy as a routine practice in all cases of stone I really cannot understand. Of course, I recognise the fact that supra-pubic cystotomy is absolutely essential in cases of large stone, or when encysted, or when we have to deal with a tumour in the bladder. Therefore my remarks only apply to supra-pubic lithotomy as a routine operation for stones of all sizes, and in patients of all ages.

The subject under consideration—the proposal to abandon the extra-peritoneal method of performing supra-pubic cystotomy, whether for stone or tumour of the bladder, and to substitute for it an intra-peritoneal operation—is, in my opinion, a very dangerous suggestion. The author calls to his aid the injection of air instead of fluid. Now this suggestion is not original; it was, I believe, suggested by Mr. Heath. (Mr. HEATH.—No, Keen of Philadelphia was the first to suggest it.) In any case, Mr. Heath wrote a paper advocating it some years ago, so that it was advanced before the present time. I do not think the suggestion has ever been acted upon, and for the simple reason it is impracticable. What do we distend the bladder for in case

of either stone or tumour? We distend the bladder, in the first instance, in order that we may more easily reach it. That may be accomplished by air, but if so, the bladder collapses almost immediately it is opened; whereas, with fluid, it takes a considerable time, after being nicked by the knife, before collapsing. That is the advantage of a fluid. You can get your finger into the bladder and examine it before it is completely collapsed. I suppose that the author has made this suggestion in order that there shall be no fluid injected into the peritoneum. I maintain that this injection of air is an utterly impossible procedure in the operation. During the operation for the removal of a tumour or stone, several quarts of fluid may be necessary, being injected through the urethra and passing out of the wound, the bladder being thus partially distended in order to enable one to perform the manipulations for removing a tumour or a stone. When the finger is introduced through the wound, you have to inject fluid from time to time in order to keep the bladder dilated and thus separate its walls from the stone or the tumour. After dilating the bladder, when you try to get the forceps on to the tumour, it often takes several minutes before you can even catch hold of the tumour, and during the whole of that time the bladder must be kept dilated more or less. I wish to point out that if you have an opening into the peritoneum it is essential that all this fluid should pass through that cavity, and no matter what number of sponges you may have, they will not prevent this fluid passing into the peritoneum and infecting it. Moreover the ureters are all the time pouring down urine, and this is mixed with the fluid. Bladders with very large stones or prostates are always very septic, and one of the advantages of irrigation by water is that you get rid of the pus and flakes of mucus adherent to its walls. Surely the author does not propose that all this fluid, laden with pus and detritus, shall be passed through the peritoneal cavity. There is one more point to which I may refer. The distance between the supra-pubic wound and the base of the bladder is already sufficiently great. That is, indeed, one of the difficulties experienced in removing the tumour, which generally grows at this situation, completely. The author's method would make this distance even greater, thereby increasing our difficulties proportionally. Under these circumstances I beg to submit that his method is not at all a practical one.

Mr. CHRISTOPHER HEATH.—I have seen the peritoneum opened by an operator when it was only intended to open the bladder, and no harm happened, but it seems to me to be rather flying in the face of Providence, when you can do the operation extra-peritoneally, to open the peritoneum for no special reason

except to get possible primary union of the wound. I do not agree with the author on that point because I never attempt to close the bladder in these cases, and I think that it is one of the advantages of the operation that the bladder has rest, and that applications can be made if necessary to the interior of the bladder so as to get it into a healthy condition. The urine is often septic, and it is not likely that primary union would result, consequently there would very likely be drainage into the peritoneal cavity with disastrous results. I think it is of the greatest advantage in most cases, though not perhaps in a child in whom the bladder wound may readily unite, but at any rate in an adult with a phosphatic stone, that the bladder should be left alone and the urine allowed to drain away, and that applications can be made to the bladder wall. The mere fact that the patient has to lie in bed for two or three weeks is of little moment if you can make sure that you have emptied the bladder as you can by this operation, and by this operation alone. It has happened to me to operate by lithotrity more than once, and to have rapid recurrence, so rapid that I was quite sure that I had not emptied the bladder. In one such case the patient passed into the hands of another surgeon, who very properly did the supra-pubic operation when he found that the reason I had failed to clear the bladder was the presence of a small pouch in which there was a stone, and the lithotrity had only dealt with the superficial part, the remainder being inaccessible. Many years ago I was one of the early surgeons to open the abdomen in a case of rupture of the bladder, and I cannot forget the difficulty I had in dealing with it. The bladder was ruptured at the back, and therefore presented more difficulty than in the operation for stone, but the practical difficulty of keeping the bowels out of the way was very great. It would be interesting to know whether the paper is entirely theoretical or whether the author has really proved the operation, and if so with what results.

Mr. A. BARKER.—I consider that the author's suggestion is a very valuable one. A good deal has been said about the risks of sepsis in these cases. In the first place the bladder should be washed out thoroughly before undertaking the operation, in the next place it would be filled with air, and lastly the bladder would not be opened until it had been pulled up with stitches into the wound and would be opened on a level with the wound in the abdomen. Under these circumstances there would be no fluid to run out. I can conceive of a stone or a tumour being taken out with the organ held up to the wound without any serious risks of sepsis, which, moreover, could be guarded against by a proper packing of gauze, etc. That puts the matter in a different light. Undoubtedly there is a danger of sepsis, but I think that is

balanced by the readier union which takes place between the peritoneal surfaces and the possibility of having complete closure once for all. In supra-pubic lithotomy, even in children, the wound may become covered with phosphates, and that is not likely to happen when the transperitoneal method is adopted. As to the difficulty of suturing the bladder, I do not think there is a parallel between the condition produced by a ruptured bladder and that of a bladder which has been forced up into the wound by inflation, the whole of it being under complete command. Of course, if there were much putridity in the bladder one would not do the operation offhand, but with careful washing out I take it that a reasonable amount of cleanliness could be produced in the bladder. We can do this in the stomach with comparatively little danger of sepsis, and there is no reason why this should not be equally obtainable in the stomach.

Mr. W. G. Spencer.—If I understand the paper aright the operation is to be an abdominal operation, for which reason the author suggests Trendelenberg's position, and from this point of view it can scarcely be looked upon as an extension of preperitoneal supra-pubic lithotomy. From this point of view, of course, one's experience is much more largely on the female side. You must deal with the organs in the pelvis as we should do with the female organs. I remember a celebrated case by Mr. Milton of Cairo, who intentionally opened the peritoneum for the removal of an extremely large stone (34½ ounces). This case supports the author's contention because the patient recovered, only to die later from stone in the kidney. No peritoneal adhesions or other evidence of harm by the operation were found post mortem. Some speakers have not taken the author's point as to the injury to the bladder which results from its being pulled up, and the peritoneum stripped off. This would be unnecessary in the abdominal operation. Other cases have been reported of rupture of the bladder, which have been sewn up. I remember one at St. Bartholomew's Hospital, under Mr. Walsham, in which there was a large peritoneal rent which healed beautifully. There are on record many cases of injury to the female bladder in operations upon the internal organs successfully sutured. I think the author's suggestion will ultimately commend itself to the members of this Society.

Sir Thomas Smith.—I owe an apology for bringing this paper before the Society without any illustrative cases. That is my misfortune and not my fault. I am no longer in a position to command beds, and in any case I should not adopt an operation of this kind without consulting my colleagues here about it. I did that thirty years ago, when I brought the kidney operation forward—an operation which I would not perform until I

had ascertained their opinion. That suggestion was even more unfavourably received than this one has been to-night. It was condemned by no less an authority than the late Sir James Ferguson. Now I do not recommend the operation; I merely bring it forward for criticism. Mr. Lucas has spoken in praise of the supra-pubic operation, and there I do not agree with him. I think it has radically failed, and as an operation it is much inferior to the old lateral operation of lithotomy. There are not many in this room who have done many lateral lithotomies, but it was at one time the best operation we had, and it is not an unsuccessful operation. Mr. Morgan has shown us that at the Children's Hospital the lateral operation was less fatal than the supra-pubic operation. It is certainly better that urine, even healthy urine, should not flow over the parts. I have sometimes distended the bladder unintentionally with air when using the hospital syringe, and I have noticed that it retained its shape. It would no doubt tend to become flaccid, but it would take some twelve or fourteen hours in doing so, and in that time, no doubt, Mr. Freyer would have been able to get the stone out. The *débris* from the bladder may, it is true, get into the peritoneum, but the bladder would have been washed out before being opened. Mr. Heath, it seems, is against the operation, but I was surprised to hear him speak so favourably of the supra-pubic operation, because he himself has done many lateral lithotomies. The supra-pubic operation is so easy that anyone who has done a post-mortem examination thinks that he is capable of doing it, and that is one of its dangers. I hope I have not wasted the time of the Society by raising the discussion. The subject is one to think over. Morrant Baker used to say that this would be the proper way to get at the bladder for stone if one could do so with comparative safety. It is now for us to discuss whether it might advantageously be done. I would ask you to bear it in mind when a suitable case comes before you. The supra-pubic operation is not intended for all stones, and there are many cases which have been mentioned which are quite unsuitable for the supra-pubic operation.

THE AFTER-RESULTS IN FORTY CONSECUTIVE CASES

OF

VAGINAL HYSTERECTOMY PERFORMED FOR CANCER OF THE UTERUS

BY

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The series of forty cases recorded in this paper includes all the cases in which I have performed vaginal hysterectomy for cancer of the uterus up to the end of April, 1899, when I completed my fortieth case. Up to the year 1893 I had for the most part treated cases of cancer of the cervix that appeared suitable for operation by the supra-vaginal amputation of the cervix, and reserved total extirpation of the uterus for cases of primary cancer of the body of the uterus.

Since that time, however, I have been more and more convinced that, to perform the supra-vaginal amputation of the cervix in such a way as to give the patient the utmost chance that the disease will not recur, is, in the majority of cases, a more difficult matter than to perform

the operation of vaginal hysterectomy. I have for some time past only performed the supra-vaginal amputation of the cervix for very early cases of cancer of the vaginal portion, in which there is a limited and superficial growth. Up to April, 1899, I have had thirty-three cases of the supra-vaginal amputation of the cervix for cancer, but I do not propose to deal with these cases in this paper.

The Cases that remain Free from Recurrence.

Among the forty cases of vaginal hysterectomy there are fourteen cases in which the disease has not recurred. In two of these, Nos. 3 and 4, in the series, although the clinical evidence convinced me that they were really examples of cancer, this cannot be proved by examination of the specimens. In the remaining twelve cases there can be, I think, no doubt whatever on this point. The specimens have been carefully examined and are here for inspection to-night, as also are sections of the growth in each case. This appears to me an important point.

My object in the present paper has been to inquire more especially into the *after-results* in the cases of cancer of the uterus in which I have performed vaginal hysterectomy. In such an inquiry it is essential, first of all, to prove that, in those cases in which the disease has not recurred, the growth was really malignant. In order to satisfy this condition I have in each case had an independent report on the growth by Mr. Targett of the Clinical Research Association, and his report will be found *verbatim* in the account of each of the cases. The necessity of a careful microscopical examination of the growth in each case is almost self-evident, and when the microscopical examination confirms the opinion based on the clinical features and physical examination, there can, I think, be no hesitation in accepting the result as fully proved.

In three cases in this series, Nos. 3, 4, and 25, the microscopic examination did not confirm the diagnosis of malignancy based on the physical examination. In

Nos. 3 and 4, though I have excluded them as "non-proven," I feel little doubt that they were cases of cancer. I have myself met with an example of cancer of the cervix in which the appearance of the growth under the microscope would certainly not have warranted a diagnosis of cancer, but in the case in question, one treated by the supra-vaginal amputation of the cervix, the malignant nature of the growth was proved by recurrence. As regards *Case No.* 25 in this series, the clinical features and the physical examination led me to believe without any hesitation that the case was one of malignant ulcer of the cervix, but on examination of the cervix by the microscope Mr. Targett reported that the case was one of tubercular ulceration. To make quite certain he examined two portions, each taken from a different part of the cervix. I think this case is an important one, as clinically it exactly resembled one of cancer of the cervix. Tubercular ulceration of the cervix as a primary condition must be extremely rare. Very little is to be found about the subject in works on gynæcology, and it has not been regarded as a condition ever likely to give rise to difficulty when the diagnosis of cancer is being considered. Yet in my case (No. 25) primary tubercular ulceration of the cervix produced a condition identical, as far as physical examination was concerned, with that resulting from malignant ulceration. I have seen a very large number of cases of cancerous ulcer of the cervix, certainly some hundreds, and I am sure that in the case in question the clinical features of the cervix were precisely similar to those produced by the ulceration of a cancerous growth. The occurrence of such a case emphasises the importance of always examining growths supposed to be cancer under the microscope before accepting them as really malignant. Again, one has occasionally heard of a case pronounced by a competent authority to be one of cancer of the cervix, where after a long time the patient gradually improved, and ultimately made a good recovery to the surprise of every one con-

nected with the case, and no doubt to the discredit of the gynæcologist who had made the diagnosis. It seems to me, in the light of the case above referred to, No. 25, that not improbably some such cases may have really been suffering from tubercular ulceration of the cervix, which presumably may occasionally get well spontaneously. However that may be, in Case No. 25, believing it to be a typical example of cancer of the cervix, I performed vaginal hysterectomy, and the patient remains quite well. It is more than four years since the operation, but I have, of course, excluded the case from Table II, the list of cases proved to be cancer of the uterus, and treated by vaginal hysterectomy, which remain free from recurrence at the present time.

To return to the question of the after-history of patients suffering from cancer of the uterus and treated by vaginal hysterectomy, in addition to proving the malignancy of the growth in each case, there is the necessity of ascertaining the state of the patient after the operation. It is not an easy thing to do. To have any real value inquiries have to be made from time to time over long periods; for instance, two cases in this paper have been kept under observation for more than seven years. The evidence of non-recurrence may be obtained either by actual vaginal examination, or by seeing the patient at intervals and observing that she continues in good health, or by hearing at intervals from her medical attendant that she continues well, or in some cases by hearing from the patient herself at intervals that she continues well. No doubt the most satisfactory thing is to examine the patient; in eight out of the twelve cases in Table II I have myself examined the patients from time to time. In some cases, however, when the patient continues well, she may not be unwilling to come to see you, but she will object to be examined, as she has nothing the matter. Two cases (Nos. 7 and 24, Table I) are in this category. In some cases one can only hear by letter from the patient, or her doctor, from time to

time. This evidence is not so unsatisfactory as it might appear, and for this reason: in those cases in which recurrence takes place the downward progress to a fatal issue is generally fairly rapid—a matter of months; so that if inquiries made at long intervals—once a year, for instance—result in a favourable report, there can be no reasonable doubt that the disease has not recurred.

Numerous cases of vaginal hysterectomy, and series of cases of vaginal hysterectomy for cancer, have been published from time to time; but I am not aware of any considerable series of such cases in which the proof both of the malignancy of the growth, and especially of the condition of the patients many years after the operation, has been given so rigorously, and in such detail, as in the present series of cases. As regards the after-histories especially, it will be seen that I have given the date on which I either examined the patient, or saw her without examining her, or heard from herself by letter, or heard from her usual medical attendant by letter.

As regards the Intervals that have elapsed since the Operation without Recurrence in the Twelve Cases referred to.

In one case (No. 7) more than seven years have passed, and the patient is known to be well.

In one case (No. 8) seven years have passed without recurrence.

Both 7 and 8 were examples of primary carcinoma of the body of the uterus.

In one case (No. 15) six years passed without recurrence.

In one case (No. 19) five and a half years have passed without recurrence.

In one case (No. 23) five years have passed without recurrence.

In one case (No. 24) nearly five years have passed without recurrence.

In one case (No. 26) nearly four years have passed without recurrence.

In one case (No. 29) more than three years have passed without recurrence.

In one case (No. 32) two years and ten months have passed without recurrence.

In one case (No. 33) two and three-quarter years have passed without recurrence.

In one case (No. 36) more than two years have passed without recurrence.

In one case (No. 39) more than one year has passed without recurrence.

Omitting No. 39, it will be seen, therefore, that there are eleven cases out of the forty remaining free from recurrence from two to seven years after the operation —that is 27·5 per cent.

This result appears deserving of close attention, since at the present time some gynæcologists have been so much discouraged by their experiences as to doubt if it is worth while to operate on cases of cancer of the uterus at all.

The comparatively high percentage of patients remaining free from recurrence in my series is, I believe, largely due to the careful selection of cases. My practice has been generally to examine the cases carefully under anæsthesia, and only to operate when the disease has appeared, so far as physical examination can decide, to be limited to the uterus.

As regards the Cases in which Recurrence is known to have taken place.

The disease is known to have recurred in 18 cases.

In 12 of them recurrence took place during the 1st year.

In 2 „ „ „ „ 2nd „

In 2 „ „ „ „ 3rd „

In 2 „ „ „ „ 4th „

The 40 cases may be divided into groups as follows:

In 12 cases there has been no recurrence.
In 18 cases there has been recurrence.
4 cases died.
In 2 cases the nature of the disease cannot be proved by examination of the specimens.
In 3 cases I have no definite information as to whether the disease recurred or not.
In 1 case the disease proved to be primary tubercular ulceration of the cervix, and not malignant disease.

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It will be seen that there were no recurrences later than during the fourth year after operation; so that when a patient has passed through four complete years without recurrence, there seems to be some probability that she may remain permanently well.

Mortality of the Operation.

There were three deaths from the operation in the series of forty cases. This represents a mortality of 7½ per cent. There was also one case which died of pneumonia three weeks after the operation. My colleague, Dr. Schorstein, who made the post-mortem examination, did not, however, consider the pneumonia to be of septic origin, and the peritoneal wound at the floor of the pelvis was healed and normal, so that I do not think this death is properly to be attributed to the operation. Still I think it right to mention it. As regards the cause of death in the three fatal cases, in Case 2 death was not due to any of the special dangers of vaginal hysterectomy, such as hæmorrhage, peritonitis, etc. It seemed that the patient could not stand a severe operation. She had a fatty heart, and died of œdema of the lungs forty-eight hours after the operation. In one case, No. 13, death was due to hæmorrhage; and in one case, No. 18, peritonitis was the cause of death. In that case forceps had

been used, as in the large majority of my cases, for securing the broad ligaments, and they were removed at the end of forty-eight hours. This interval is certainly sufficient as regards security from hæmorrhage, but it may not be always sufficient to prevent the breaking down of the recent adhesions that shut off the general peritoneal cavity from the region of the wound when the forceps are being removed. Case No. 18 was doing perfectly well till the forceps were taken off. While this was being done she suddenly complained of sharp pain in the abdomen, and from that time began to do badly, symptoms of peritonitis appeared, and she died on the seventh day. I believe the cause of the peritonitis was that the adhesions shutting off the general peritoneum were broken down in taking off the forceps, and the region of the wound, which is always in a foul, sloughy condition at this stage of the case when pressure forceps have been used, was thus put into communication with the peritoneum. Since that case I have generally left the forceps on for either three or four complete days in order to allow time for the protecting adhesions to become firm.

Some Points in the Technique of the Operation.

The mode of securing the broad ligaments.—Various instruments, special forms of pressure forceps, and special kinds of clamp have been invented and used for securing the broad ligaments. I have never used any special instrument for this purpose, but have always used Wells's pressure forceps, large or small, according to circumstances. In a few of my earlier cases (Nos. 1, 2, and 3) I used no pressure forceps, but relied entirely on ligatures. Since then I have always used Wells's forceps; occasionally a ligature or two have been used as well, but not often.

The posterior vaginal wall.—The cut edge of the posterior vaginal wall often bleeds rather freely. As a rule, after opening Douglas's pouch I pass sutures with a

Hagedorn's needle from the vaginal wall near the cut edge to the peritoneum and back again, so as to be able to tie the cut edge in some two or three sections. This at the same time avoids a wide separation of the peritoneum from the posterior vaginal wall. There is much loose tissue between these structures, and they separate easily to a considerable extent. This is avoided by suturing in the manner described.

Use of the cautery.—Although I now prefer vaginal hysterectomy to supra-vaginal amputation of the cervix, except in early cases of cancer of the vaginal portion, partly because it is an easier operation and partly to avoid the chance of subsequent dysmenorrhœa, which occasionally follows supra-vaginal amputation owing to contraction of the cicatrix, yet it is well to bear in mind that it is more especially in the direction of the vagina and of the connective tissue round the cervix that cancer of the cervix tends to spread. Only rarely does it spread to the body of the uterus, at least till such a late period in the case that complete removal of the diseased tissues has become obviously impossible.

I believe it is a good plan when operating for cancer of the cervix, after the cervix has been freed, to apply Paquelin's cautery to the cut surfaces adjacent to the growth. I have done this in all except a few of my earlier cases.

Some Complications of Vaginal Hysterectomy.

Secondary hæmorrhage.—In only one case (No. 39) have I found bleeding occur *immediately after* removing the forceps. The bleeding was not much, but I thought it better to expose the upper part of the vagina with a Sims's speculum, and secure the bleeding point with another pair of Wells's forceps, which was left for two days longer. No subsequent trouble occurred. It is clearly an unusual accident.

Secondary hæmorrhage at a later period occurred in Case 28; this was actually at the end of the third week, and required large pressure forceps to control it. In all cases where forceps have been used the tissues at the upper part of the vagina by the time the forceps are taken off, and until some two or three weeks after the operation, are in a sloughy condition. If secondary hæmorrhage should occur at any time during this period, great care is necessary when applying forceps to stop it to take up nothing more than is absolutely required to secure the bleeding point. The vaginal portion of the cervix—the usual familiar landmark—is of course absent, and a portion of the bladder, or one of the ureters, may be easily picked up. Fortunately secondary hæmorrhage, either when the forceps are taken off or subsequently, is very uncommon. I have only met with it in the two instances mentioned in the series of forty cases.

Injuries to ureters.—The only case in which a ureter was injured was No. 28, the case in which secondary hæmorrhage occurred at the end of the third week. As mentioned above, pressure forceps were applied and left on for two days. Not long after removing them the patient began to suffer from incontinence of urine. When the raw surface of the top of the vagina had healed, this incontinence still continued. I thought at first it might be due to a vesico-vaginal fistula. When, however, the bladder was filled with milk, while the vagina was fully exposed with a Sims's speculum, none of the milk came through into the vagina, but the flow of urine still continued. It was thus evident that the incontinence was due to a ureteral fistula. The patient was unwilling to have anything done at that time, and I saw nothing of her for several months. She then one day came up to the ward to tell me that she was quite dry, and had been so for some time. I examined her, and found no sign of incontinence. I have seen her several times since, and there has never been any sign on examination of anything wrong with either of the kidneys.

In Case 4 the patient suffered from hæmaturia for some days. The urine was bloody when drawn off with the catheter. This condition gradually disappeared, and the urine became normal. The hæmaturia may possibly have been caused by reflex congestion of the kidneys, due to a portion of a ureter, or of the bladder, having been nipped by the pressure forceps. She had no incontinence of urine, and remains quite well, nearly ten years since the operation, so that no permanent damage could have been done.

Injuries to ureters have not been, as far as I have been able to ascertain, so very rare in the history of vaginal hysterectomy, but the case mentioned (No. 28) is the only one in which the accident has happened in my own practice. Nor have I met with any cases where the ureters have been injured among my thirty-three cases of supra-vaginal amputation of the cervix—an operation in which there is practically the same chance of injuring the ureters as in vaginal hysterectomy.

Injuries to the bladder.—I have not had a case where the bladder has been accidentally injured, either among my vaginal hysterectomies or among my cases of supra-vaginal amputation of the cervix. I have, however, seen a bad case of vesico-vaginal fistula after a vaginal hysterectomy, said to have been performed in South America.

Cases suitable for vaginal hysterectomy.—When there is evidence that the disease has spread beyond the anatomical limit of the uterus in any direction, it is, I believe, hopeless to expect any permanent benefit from vaginal hysterectomy, even if it is possible to perform the operation. In many cases it is at once evident on examination that the growth has spread far beyond the uterus. No difficulty arises in coming to a conclusion in such cases. In other cases, where, on an ordinary examination, the mobility of the uterus appears to be unimpaired, it is not so easy to decide. The uterus may be freely movable, yet the base of the bladder may be

involved. Again, the mobility at an ordinary examination may seem normal, yet when an attempt is made to draw the cervix down to the vulva a check is felt at one side or the other in the region of the broad ligaments, or of the utero-sacral ligaments, due to the extension of the malignant growth in the corresponding direction. This extension can generally be best appreciated by examining *per rectum* while the cervix is being drawn down with a volsella.

Cases of this kind are certainly unsuitable for radical operation. It may be possible to remove the uterus, but that is of little use if a portion of broad ligament or utero-sacral ligament, infiltrated with the malignant growth, is left behind.

In most of these doubtful cases the best plan is to make a careful examination under anæsthesia before deciding as to operation.

For my own part, I have never felt it to be justifiable to perform an operation like vaginal hysterectomy as a palliative operation,—in other words, to perform it where one feels certain that the patient has not even a chance of obtaining any permanent benefit.

On the other hand, there may be a very extensive growth, and yet, if it does not seem to have extended beyond the uterus, operation is advisable. One must not be too ready to reject cases as hopeless. Case No. 22 in this series is a good example of this. The growth from the cervix was a very large one of the "cauliflower" type, and yet she certainly remained well for more than three years after removal of the uterus. I am not even certain that she had recurrence, as, though she is dead, she died in America a comparatively short time after I last examined her, and there was then no sign of recurrence.

Again, No. 19 had been told at another hospital that her case was too advanced for operation, yet she remains well more than five years after the operation. In No. 15 also, though the growth is obviously a large one,

the patient remained free from recurrence for six years, when she died of phthisis. No. 23 is another instance in point; the growth is a large one, but she remains well five years after operation. These cases, then, Nos. 15, 22, and 23, go to show that the size of the growth from the cervix is relatively of small importance, and that the essential point is whether there is any extension to the tissues outside the uterus itself.

I have arranged the cases in two tables.

Table I is a list of the forty vaginal hysterectomies for cancer which I had performed up to April, 1899, with some of the more important details of the cases.

Table II is a list of the twelve cases in which the disease is known not to have recurred.

Notes of the cases in Table II are also given.

Conclusions.—The conclusions that appear to follow from a consideration of the facts in this paper are—

1. That in a certain proportion of cases patients suffering from cancer of the uterus may be relieved by operation for periods of many years; in some cases for so long a time, seven years and upwards, that there seems some probability that the relief may be permanent.

2. That the proportion of cases in which this result can be expected must remain very small so long as cases generally only seek advice at a late stage of the disease; and that consequently—

3. The great desideratum is early diagnosis. Improvement in this direction depends to some extent on a better appreciation, on the part of women themselves, of the early symptoms of the disease, and especially of the significance of bleeding after the menopause, or of bleeding occurring at an earlier time of life between the menstrual periods.

Early diagnosis, of course, also depends partly on the profession. Especially important is the general recognition of the gravity of the symptom just mentioned. It is equally important also to bear in mind that patients suffering from cancer of the uterus may, and generally do,

for a relatively long period *look* quite well. They may be well nourished, or not infrequently even excessively fat; and, as regards the aspect of the face, they may appear to be in perfect health.

Notes of the twelve cases (Table II) in which the disease has not recurred.

Case 7. Mrs. D— (with two illustrations).—The patient was 53 years of age. She had been married twenty-one years; she had had no children, but two miscarriages, each at about three months, the last thirteen years before I saw her. I was asked to see her in consultation with Dr. Godson and Dr. Stott, of 1, Highgate Road, N.W. The symptoms were continued hæmorrhage for seven or eight months, with occasional profuse losses of blood and severe pain in the hypogastric region. On examination the uterus was found to be moderately enlarged and freely movable. The vaginal portion of the cervix was normal. The sound occasioned very free bleeding. It was agreed that the best course would be to dilate the cervix and examine the endometrium. This was accordingly done. Two specially prepared laminaria tents were inserted, and the next afternoon the dilatation of the cervix was completed with Hegar's dilators under anæsthesia. There was a hard, irregular condition of the inside of the body of the uterus. Nothing could be detached either with the finger or with a curette. The diagnosis rested on the symptoms, and on the fact that the condition of the endometrium could not be classified as belonging to any non-malignant state. I advised that vaginal hysterectomy should be performed, and I performed the operation on February 1st, 1893, assisted by Dr. Godson, Dr. Stott, and Dr. Sequeira, who was resident accoucheur at the London Hospital at that time. Mr. F. W. Braine gave the anæsthetic. The patient made a good recovery. A section from the uterus was made by the Clinical Re-

search Association, and reported on by Mr. Targett as follows:—"The growth of the uterus (Mrs. D—) is a columnar-celled carcinoma of the body, of the villous type. It has deeply invaded the muscular substance."

A drawing of the uterus, and of the sections, accompany this paper. The patient came to see me on June 8th, 1900, just to show me that she was quite well. The interval in this case without recurrence is, therefore, seven years and four months. Her present medical attendant is Dr. Andrew Brown, of 27, Lancaster Road, Belsize Park.

Case 8 (with two illustrations).—L. S—, a married woman aged 57, was admitted under my care into the London Hospital on May 1st, 1893. She was sent up to me by Dr. Best, of Dover.

Previous history.—She was born at Blackburn, in Lancashire. During her infancy her family removed to Crayford, in Kent. Her circumstances have always been comfortable. She had scarlet fever in childhood, and cholera in 1849.

Menstruation.—The catamenia began between fourteen and fifteen. There was some irregularity for the first ten months, but after that she was very regular every four weeks, and did not lose very much. She always suffered a great deal of pain after the periods. She was married at the age of thirty-three, and had six children, but no miscarriages. The last confinement was fourteen years ago.

Present illness.—About two years ago the periods began to be irregular. She would "see nothing" for two or three months, and then a period would come on with an excessive loss, containing clots. During the last eighteen months she has been losing blood constantly, and for the same time has suffered a good deal of pain, more severe at night, in the lower part of the abdomen. She was closely questioned as to the time when the various symptoms arose, and it became clear that as long ago as

two years there was a red discharge between the periods, and that for the greater part of the last two years she had had a good deal of pain in the back and lower part of the hips. She said also that she always had suffered a great deal of pain during her periods from the time they began. As she grew older the pain at the periods was not so severe until about two years ago, when it recommenced. The pain during this two years has been constantly present, and has increased in severity.

Present state (May 1st, 1893).—She was a stout, heavy woman, and, as regards the appearance of the face, she did not look very ill There was no cachexia. Her weight on admission was 12 st. 13½ lbs.

Nothing abnormal could be felt on examination of the abdomen.

On vaginal examination there was a considerable descent of the anterior vaginal wall, which protruded from the vulva. There was an extensive rupture of the perinæum, reaching back to the edge of the sphincter. There was also slight prolapse of the rectal mucous membrane. Through the speculum the vaginal portion of the cervix appeared healthy. The uterus was fairly movable, and in the normal position. The body of it was somewhat enlarged, and the sound passed 3¼ inches, causing rather free bleeding.

She was kept under observation in the hospital during the whole of May, and during that time there was a constant red vaginal discharge, and she complained of pain about the lower part of the abdomen, more severe at night.

On May 31st, at 5 p.m., two specially prepared laminaria tents were inserted into the uterus with strict antiseptic precautions, and on the following day (June 1st), at 2 p.m., she was anæsthetised with ether. The tents were removed, and it was found that the cervix admitted the index finger easily. The uterus was drawn down to the outlet with a volsella. The finger was passed into the uterus, and detected a hard, irregular condition of the

endometrium ; this was particularly marked at the upper part and to the right. I could not classify the condition as resembling any non-malignant pathological state, and I came to the conclusion that the case was one of primary carcinoma of the body of the uterus. I should have mentioned that nothing could be scraped away from the endometrium with a curette.

Operation (June 8th, 1893).—The patient was anæsthetised with ether, and placed in the lithotomy position. The vulva and vagina were thoroughly disinfected with perchloride lotion 1 in 1000. Having drawn down the cervix, the anterior fornix was incised first, and the bladder separated from the cervix as high as the internal os. The posterior fornix was then similarly incised, and Douglas's pouch opened. The cervix was cleared laterally as high as the level of the internal os, pressure forceps being used to control the bleeding where necessary. The utero-vesical pouch of the peritoneum was then opened. The remaining lateral attachments were clamped piece by piece, the left broad ligament being first secured and divided. The uterus was then, as it were, delivered, the left side of it first, so that at this stage it was hanging by the right broad ligament. The latter was then secured with pressure forceps and divided. The uterus was then removed. The vagina was filled with iodoform gauze, the upper part of the plug projecting for an inch or so into Douglas's pouch.

The patient's progress after the operation was very satisfactory. The highest temperature in the first week was 100·8° on the evening of June 11th. On one occasion in the second week (June 16th) it reached 101·4°. After June 20th the temperature was practically normal, only once after that date reaching 100°. The pressure forceps were removed on the afternoon of June 10th.

The patient went home on July 21st, 1893.

I have seen her every summer since the operation, and have examined her. So far she has remained free from

any sign of recurrence, and appears to be in perfect health.

Sections for examination under the microscope were prepared by the Clinical Research Association, and reported on by Mr. Targett as follows :—"This growth from the body of the uterus is a columnar-celled carcinoma, in which the tubular arrangement of the cells is well preserved. The tissues have shrunk in hardening, but the sections are sufficiently good for microscopic drawings."

A drawing of the uterus and drawings of the sections accompany this paper.

The last time the patient was examined was on July 19th, 1900, at the London Hospital. There was no sign of recurrence, and she was quite well.

Case 15 (with one illustration).—Mrs. J—, a married woman aged 57, was seen by me in consultation with Dr. Howse, then of Barking Road, E., but now of Reading, in February, 1894.

She had had thirteen children, the last fifteen years ago, and two miscarriages some time before the last confinement. The complaint when I saw her was that she had been losing blood from the vagina for the last eight weeks. Before this appeared there had been a yellow vaginal discharge for nine months. She had had no pain. She thought she had lost flesh, and said her appetite was bad. The menopause occurred at fifty-one.

On examination there was found a large "cauliflower"-like growth springing from the vaginal portion of the cervix, forming a ring of soft projecting growth round the os uteri, and bleeding readily on examination.

It was decided to make a thorough examination under anæsthesia, with the understanding that, if the conditions were found favourable, the uterus should be removed. Accordingly, on February 27th, 1894, the patient was anæsthetised. It was then found that the uterus could be drawn easily down to the vulva, and that the growth did not seem to have spread beyond the limits of the cervix.

There was a ring of apparently healthy vaginal portion outside the malignant growth all the way round it. This can be well seen even now in the specimen.

The uterus was accordingly removed, the steps of the operation being much the same as in the preceding case, except that Paquelin's cautery was very freely applied to the cut edges of the vaginal fornices and neighbouring tissue from which the cervix had been detached. The patient made a very good recovery.

I heard of her from time to time from Dr. Howse. She remained free from recurrence. He saw her several times in the course of her last illness (phthisis), and there was no return of the cancer up to the time of her death, which occurred in February, 1900, and was due to phthisis. Dr. Howse had attended her many times in former years for lung trouble.

The interval since the operation without recurrence is therefore in this case *six years*.

Sections of the growth for the microscope were prepared by the Clinical Research Association, and reported on by Mr. Targett as follows:—"The second portion of this growth (Mrs. J—) has been examined, but the tissue is so necrotic that the sections are not worth drawing. The nature of the growth is undoubtedly squamous-celled epithelioma, but owing to decomposition the cells are much vacuolated, and the tissue has therefore an unnatural spongy appearance. It is not worth the expense of a drawing." I may add that the uterus had been more than five years in spirit before Mr. Targett had a piece of the growth for sections.

A drawing of the uterus accompanies this paper.

CASE 19 (with two illustrations).—E. S—, a married woman, 52 years old, was admitted under my care into the London Hospital on October 9th, 1894. She had had two children, the last one twenty-six years ago, but had never had any miscarriages.

For the last eight years she had been a monthly nurse.

She has always enjoyed good health, and there is no history of any previous illness. She has always had a comfortable home. She has been a teetotaler all her life, and has always lived in or near the East End of London. Her two children were born within three and a half years of her marriage.

Menstrual history.—The catamenia appeared when she was thirteen years old, and she was always regular every four weeks except when pregnant. She always suffered very much from headache at the menstrual periods. The menopause occurred five years ago, *i. e.* in 1889. After the menopause she "saw nothing" till the end of June, 1894, when, on awaking one morning, she found that she had lost a considerable quantity of blood during the night. Throughout the whole of July, 1894, she continued to have a series of losses, which occurred irregularly, the discharge being blood-stained and offensive. Occasionally it ceased altogether for two or three days. In August there was much less discharge, but since then, and up to the present time, it has continued more or less. She has been able to continue at her work.

She consulted Dr. Howse, then of Barking Road, now of Reading, in September, 1894, and afterwards was an in-patient at the Samaritan Hospital for four days. She said she was told there that the disease was too far advanced for any operation to be advisable.

A month before her admission to the London Hospital, *i. e.* October, 1894, she first noticed a pain in the left iliac and in the hypogastric regions. It was of a burning character, not relieved by lying down, and not worse at night. The pain has gradually become more severe. A week before her admission she began to feel a pricking and shooting sensation in the left breast. She said she had not been getting thinner.

State on admission.—She was fairly well nourished, but rather sallow. On October 11th (1894) she was examined under anæsthesia. On vaginal examination there was no obvious projecting growth, the only sugges-

tive point on gentle examination being that the external os was unusually patulous. On pressing the finger firmly into the os a soft friable growth could be felt occupying the cervical canal. The uterus was drawn down to the vulva with volsellæ, and came down easily. The vaginal fornices seemed to be free from any infiltration. On examining bimanually no extension of the disease into the broad or utero-sacral ligaments could be made out.

Operation (October 13th, 1894).—The patient was anæsthetised with ether, and placed in the lithotomy position. Vaginal hysterectomy was then performed. Wells's forceps were used for securing the vessels. The vagina was packed with iodoform gauze, and the upper part of the gauze plug was pushed into the pouch of Douglas. The gauze and forceps were removed ninety-six hours after the operation, but no vaginal douches were given till the 24th, when she was ordered vaginal douches of weak iodine water twice daily. The temperature after the operation did not rise above 100·4°, and the patient made an uninterrupted recovery.

Examination of the uterus after removal.—The body of the uterus was not appreciably enlarged, and, so far as could be judged by the naked eye, the disease had not extended into it. An interesting point, however, was that at one part of the fundus there was a white nodule of circular shape, the size of a pea, in the thickness of the uterine wall. Microscopical examination of this nodule subsequently showed that it was a small fibromyoma.

Sections of the cervix were prepared by the Clinical Research Association, and were reported on by Mr. Targett as follows:—"The substance of the cervix uteri is infiltrated with branching processes of squamous-celled epithelioma. There are a few cell-nests, and some of the larger processes show granular degeneration of the central cells. The section is suitable for drawing."

Two drawings of the section accompany this paper.

I saw this patient last on March 15th, 1900, at the

London Hospital, and examined her. The scar was quite healthy, and she was herself perfectly well. The interval since the operation in this case is, therefore, five years and a half.

Case 23 (with three illustrations).—Mrs. H—, 55 years of age, was brought to see me by Dr. Garry Simpson, of East Acton, on May 17th, 1895. She had had six children, the last seventeen years previously, and two miscarriages, both before the date of the last confinement.

The menopause occurred at the age of fifty. Since then she had "seen nothing" till August, 1894. Since that time there has been a constant red discharge from the vagina, and for the last two or three weeks the discharge has been offensive. She felt ill and worn out at the time when the vaginal discharge commenced. For some time she has suffered from continuous pain in the lower abdomen; the date of its commencement could not be fixed. Of late she has been getting rapidly thinner.

On examination of the abdomen nothing abnormal could be felt. On vaginal examination a large "cauliflower" growth was felt springing from the vaginal portion of the cervix; the uterus seemed freely movable, and the body of the uterus seemed considerably larger than normal in a woman past the menopause. She went into Fitzroy House for the purpose of having the uterus removed, and during the time—a few days—she was there before the operation the temperature at night was 100°, or thereabouts, as a rule.

Operation (June 1st, 1895).—Vaginal hysterectomy was performed in a manner similar to that already described in the preceding cases. At one stage of the operation the whole field became suddenly inundated with horribly fœtid pus. This came from the body of the uterus, and had been let out by a laceration about the junction of the cervix and body caused by traction with

the volsella. The pus had previously been pent up in the body of the uterus by occlusion of the os internum, constituting the condition known as *pyometra*. In spite of the fact that the whole region of the wound was fouled with this fœtid pus the convalescence was quite uninterrupted.

This patient writes to me every year on the anniversary of her operation. As she is now living in Australia, I do not actually get the letter for some weeks afterwards. I have had a letter from her this year (1900) dated June 11th, and in it she says that she still continues quite well. The uterus shows well the enormous distension of the cavity of the body by the pus referred to above, and it also shows an extensive cauliflower-like growth from the cervix extending up the cervical canal to the internal os. A portion of the cervix was sent to the Clinical Research Association for microscopical examination, and Mr. Targett reported on it as follows:—"The growth from the cervix uteri is a squamous-celled epithelioma of the papillary type. There is a considerable amount of keratoid change in the epithelial processes."

A drawing of the uterus and two drawings of the section accompany this paper.

Case 24 (with two illustrations).—Mrs. A. H—, a married woman aged 48, was admitted under my care into the London Hospital on the 21st of August, 1895, at the request of Dr. Aspland.

Previous history.—She had been married twenty-one years, but had been a widow for fifteen years. She had never been pregnant. The catamenia appeared when she was about fifteen years old. She had dysmenorrhœa while she was single, but suffered much less from this after her marriage. The menopause occurred about three years ago.

Present illness.—She has not been well for some time. For the last seven or eight months she has had a yellow vaginal discharge, which has been mixed with blood more

often than not. She had no pain when the discharge began, but for the last two months she has had pain in the left iliac region occasionally. It has gradually become more severe, and is also felt at times across the lower abdomen, and in the lower part of the back. It was clear, however, that a blood-stained discharge, and a feeling of not being in good health, were for some months the only symptoms. She said on admission that she felt weaker than formerly, but did not think she had lost flesh. Her appetite latterly had not been good.

State on admission.—Nothing abnormal was detected on examination of the abdomen. On vaginal examination some blood-stained discharge was seen about the vaginal orifice, and in the vagina. It was not offensive. The uterus was found to be strongly retroverted; the vaginal portion of the cervix was rather soft, but otherwise normal. The uterus was easily replaced with the sound, which passed three and a quarter inches. On bimanual examination the uterus was found to be freely movable, and the body of it uniformly enlarged.

On August 23rd two small laminaria tents were put into the cervix, and on the next day the dilatation of the cervix was completed under anæsthesia with Hegar's dilators up to No. 19.

On passing the finger into the uterus a growth about the size of a walnut was found projecting from the posterior wall. It had a papillary surface, and was very friable, portions being easily broken off with the finger.

Operation (August 30th, 1895).—Vaginal hysterectomy was performed, the steps of the operation being similar to those adopted in the preceding cases. The pressure forceps and gauze were removed on the fourth day, and the patient made an uninterrupted recovery, leaving the hospital on the 23rd of September.

A portion of the growth was sent to the Clinical Research Association for microscopical examination, and Mr. Targett reported on it as follows:—"The growth from the body of the uterus is a soft glandular-celled

carcinoma, which has extensively infiltrated the muscular substance. The growth is of the columnar-celled type, though the tubular arrangement of the cells is not recognisable in the section."

I had a letter from this patient in May, 1900, to say that she was still quite well. The interval since the operation is therefore nearly five years.

CASE 26 (with two illustrations).—E. S—, a married woman aged 35, was admitted into the London Hospital under my care on April 6th, 1896. She was sent to me by Dr. Dunlop, of Purfleet.

She had been married sixteen years, and had had eight children, the last eight months old. She had had one miscarriage five years previously. Menstruation had always been natural.

History of the present illness.—She has found herself getting thinner lately, and has had a bad appetite. About three months ago she consulted a doctor on account of a yellow vaginal discharge, which she had had for some months. During the last two months the discharge has increased in quantity, and has been sometimes blood-stained. She has sometimes felt a pain in the lower abdomen and back, but pain did not seem to have been a marked feature in her present illness.

On April 10th she was examined under anæsthesia. On vaginal examination a "cauliflower-like" growth was seen springing from the vaginal portion of the cervix. The cervix could be easily drawn down to the outlet of the vulva with a volsella, and there was a good margin of apparently healthy tissue round the growth. The body of the uterus was not enlarged. The case seemed a suitable one for radical operation.

Operation (April 16th, 1896).—The patient was anæsthetised with the A.C.E. mixture. Vaginal hysterectomy was then performed, the method adopted being similar to that described in the preceding cases. The cut margin of the vaginal wall round the cervix was thoroughly

seared with Paquelin's cautery. The patient made an uneventful recovery, and went home on May 23rd, 1896.

A portion of the growth was sent to the Clinical Research Association for microscopical examination, and Mr. Targett reported on it as follows :—"This portion of the cervix uteri is thickly infiltrated with a soft squamous-celled epithelioma. There are no typical cell-nests, but a considerable number of cell-inclusions."

I have seen this patient several times since the operation; the last time I examined her was on October 12th, 1899, when there was no evidence of recurrence. I have also seen her on March 15th, 1900, when she said she was quite well, but I did not examine her on that occasion.

The interval since the operation in this case is, therefore, nearly four years.

Case 29.—E. W—. This was the case of primary sarcoma of the body of the uterus which formed the subject of a communication read before the Obstetrical Society of London, and which was published in vol. xxxix, p. 246, of the Society's 'Transactions.'

I only refer to it here for the purpose of recording her subsequent progress. I have seen her this year (1900), more than three years since the date of her operation, and she remains free from any sign of recurrence.

Case 32.—Mrs. B—, aged 61, was sent to me by Dr. Pope, of Kington, Hereford. She had been married many years, and had had two children, the last twenty-eight years ago. I saw her on August 19th, 1897. She gave a history that nine years ago she had a fall, and that there had been more or less discharge, occasionally blood-stained, from the vagina since.

For the last two months there had been a constant discharge of blood every day. About a week before I saw her she had had a flooding, and was said to have lost about a pint of blood.

The menopause was said not to have occurred. She had not been getting thinner.

On August 20th she was examined under anæsthesia. There were several mucous polypi hanging from the cervix. The uterus was considerably enlarged, and was freely movable. As I did not think the mucous polypi could have accounted for the flooding mentioned above, I dilated the cervix and found a growth in the endometrium, a portion of which was detached for examination, and sent to the Clinical Research Association.

Mr. Targett reported on it as follows :—"The tissue from the body of the uterus is extensively infiltrated with a soft columnar-celled carcinoma. The tubular arrangement of the cells is generally well preserved, but in certain parts of the section the growth has undergone caseation."

The patient was accordingly advised to have the uterus removed.

Operation (September 4th, 1897).—Vaginal hysterectomy was performed as in the preceding cases ; the patient made a good recovery. I examined her last on July 7th, 1900. She was quite well, and there was no sign of recurrence. The interval since the operation is, therefore, two years and ten months.

Case 33.—E. R—, a married woman aged 38, was admitted under my care into the London Hospital on September 4th, 1897.

She had been married nineteen years, and had had six children, the last three years ago, and two miscarriages, the last nine years ago.

The catamenia appeared when she was sixteen. The periods lasted four days, and were preceded by severe pain for three days, relieved on the appearance of the flow. She was never regular every four weeks till the last four years, but since the last confinement she has been fairly regular till recently.

Present illness.—This began nine weeks ago, when bleeding occurred, and continued for nearly five weeks.

After an interval of three or four days she had a flooding, and the loss of blood continued for eight days. She has had no pain, but has been getting thinner the last six weeks, and her appetite during that time has been poor.

On examination (September 5th, 1897) there was seen some blood about the external genitals. There was slight prolapse of both vaginal walls. There was marked enlargement of the anterior lip of the cervix, which was three or four times as thick from before backwards as the posterior lip. The growth on the anterior lip was raised, and in shape like a horseshoe with the convexity forwards. The growth bled easily on examination, and the sound pressed against it readily penetrated its substance. The body of the uterus was of normal size, and the uterus was freely movable.

Operation (September 6th, 1897).—Vaginal hysterectomy was performed, as in the preceding cases. She made a good recovery, and left the hospital on October 1st, 1897. Sections of the growth were prepared by the Clinical Research Association, and reported on by Mr. Targett as follows:—"The substance of the cervix uteri is extensively invaded with thick branching processes of squamous-celled epithelioma."

I last examined this patient on the 21st of June, 1900, at the London Hospital. She was then quite well, and there was no sign of recurrence. The interval since the operation without recurrence is therefore two years and nine months.

Case 36.—E. M—, a married woman aged 46, was admitted into the London Hospital under my care on November 27th, 1897. She was sent to me by Dr. Honnywill, of Sutton, Surrey.

She had been married twenty-seven years, and had had four children, the last nineteen years ago. She had a flooding in the last week of August, 1897; the loss of blood continued for three weeks; there was then an interval of three weeks without any loss. The bleeding then began

again, and since then she has been losing blood almost constantly. She thought she had been getting stouter.

On examination it was found that the anterior lip was the seat of a growth about equal to half a crown in area. The growth was raised, and had an overhanging margin. The whole anterior lip from before backwards measured $1\frac{3}{8}$ inches, the posterior lip similarly only $\frac{3}{8}$ of an inch. The sound pressed against the growth readily penetrated its substance. Two small hard nodules were felt under the mucous membrane, one to the right of, and the other above the growth. The uterus was freely movable, and there was no evidence of extension of the disease to the broad ligaments or utero-sacral ligaments.

Operation (December 2nd, 1897).—Vaginal hysterectomy was performed, the method adopted being the same as in the preceding cases. Paquelin's cautery was used to sear the cut edges of the vaginal walls. There was slight pyrexia for the first fortnight after the operation, the highest point reached being 101° on the evenings of December 6th and 7th. After the 7th the temperature was normal. The patient did well, and went home on December 29th.

A portion of the cervix was sent to the Clinical Research Association for examination, and Mr. Targett reported on it as follows:—"The growth in the cervix uteri is a malignant adenoma, that is a columnar-celled carcinoma in which the cells preserve their tubular arrangement. The tissues are deeply invaded, and there is much small-celled growth around the proliferating tubules."

I last examined the patient on March 22nd, 1900, at the London Hospital. There was no sign of recurrence, and she expressed herself as feeling quite well. The interval since the operation is therefore two years and nearly four months.

CASE 39.—Mrs. J. R—, a married woman aged 36, was admitted under my care into the London Hospital on February 4th, 1899. She had had eight children, the last

eleven months prior to her admission. She had also had two miscarriages.

Her chief symptom had been a red vaginal discharge, which had been present fifteen months. At times the bleeding has been severe. She had also had pain in the left iliac region for ten months. She was suckling at the time of her admission.

On February 9th, 1899, the following note was made:—"On the vaginal portion of the cervix is a raised and slightly irregular crescentic growth. It involves chiefly the left side of the vaginal portion immediately adjacent to the external os, and about two thirds of the posterior lip. It has an overhanging margin. About the middle of the anterior lip a little nodule, the size of a shot, is felt under the mucous membrane, the surface of which over the nodule is healthy. There is another similar nodule to the left of the first. There are also two nodules to the right under the mucous membrane of a similar character. The sound pressed against the crescentic growth enters its substance to the depth of an inch. The uterus is freely movable, retroverted, and its body not enlarged. There is no evidence that the growth has extended beyond the limits of the cervix."

Operation (February 16th, 1899).—Vaginal hysterectomy was performed in the same way as in the preceding cases, Paquelin's cautery being used to sear the cut edges of the vaginal wall. The forceps were removed on the 20th. Slight bleeding occurred, so that the region of the wound was exposed with Sims's speculum. A pair of Wells's small pressure forceps was used to secure the bleeding point. This pair was left on two days, and then removed. No further bleeding occurred. The temperature only rose above 99·5° on two occasions; one was on the evening of the 20th, and the other on the evening of the 22nd, when the temperature was 100·2° and 100° respectively. The patient went home on the 15th March.

A portion of the growth was sent to the Clinical Research Association for microscopic examination, and

Mr. Targett reported on it as follows:—"The cervix of J. R— is very extensively invaded with squamous-celled epithelioma. Some of the epithelial processes are large, and the central cells have undergone granular degeneration. In others there are small cell-nests."

I examined this patient on July 26th, 1900, and found no sign of recurrence. The interval since the operation in this case is therefore one year and five months.

TABLE I.—*Forty Consecutive Cases of Vaginal Hysterectomy performed for Cancer of the Uterus.*

No.	Name.	Disease.	Date of operation.	Place.	Immediate result.	Remarks.	Age.	Remote result.
1	Mrs. R.	Cancer of body	Mar. 1st, 1886	London Hospital	Recovered	Ligatures only used to secure broad ligaments	58	Recurrence early in 1887. Died July 7th, 1887, 16 months after the operation. (Recurrence during the first year.)
2	Mrs. M. M.	Cancer of cervix	Oct. 4th, 1886	London Hospital	Died 48 hours after operation	The body of the uterus was moderately distended with pus (pyometra), which was set free in the course of the operation. There was no local complication such as hæmorrhage or peritonitis. The wall of the right ventricle was very thin and the heart fatty. The patient died from œdema of lungs and heart failure. Ligatures only to broad ligaments	62	—
3	Mrs. W.	Cancer of body	Nov. 7th, 1889	London Hospital	Recovered	Large soft "cauliflower" mass protruding through widely dilated os on admission. This was removed immediately, and vaginal hysterectomy performed on a subsequent occasion. None of the original "cauliflower" mass was kept for examination, as it was expected that the uterus would show more of the malignant tissue. This was not the case; so that, although on clinical grounds I am certain the soft friable mass removed was malignant, I cannot prove it by microscopical examination. Ligatures and pressure forceps to broad ligaments	42	Seen and examined Oct. 5th, 1893, *i. e.* nearly 4 years after operation, when there was no recurrence. Not seen since.
4	Mrs. D.	Cancer of	Oct. 23rd, 1890	London Hospital	Recovered	Definite "cauliflower" growth on posterior lip of cervix. An interesting	41	This patient has been regularly seen up to and including the present

		cervix				feature was the occurrence of hæmaturia soon after the operation, lasting 5 days. Blood casts were present. Pressure forceps used to broad ligaments. Clinical signs and symptoms seemed conclusive as to malignancy, but the microscopic examination of the growth was not conclusive on this point		year 1900. There has been no sign of recurrence.
5	Mrs. J. T.	Cancer of body	March 17th, 1892	London Hospital	Recovered	Soft papillary growth projecting in cavity of body of uterus	44	This patient remained free from recurrence for more than 2½ years after the operation. Within the next 6 months, however, recurrence was ascertained by examination to have taken place. The case is fully recorded in Lond. 'Obst. Soc. Trans.,' vol. xxxvi, p. 374. (Recurrence during the third year.)
6	Mrs. B.	Cancer of cervix	June 16th, 1892	Private; with Dr. Russell, of Upton Park	Recovered	Little of the growth to be seen at the os uteri. The whole of the cervical canal up to the internal os was affected by the malignant growth; the cervix, in fact, converted into a thin shell lined with the growth	59	Good health for 2½ years after operation, then recurrence took place in the scar. (Recurrence during the third year.)
7	Mrs. D.	Cancer of body	Feb. 1st, 1893	Private; with Dr. Stott, of Highgate, and Dr. Godson	Recovered	An example of "hard" cancer of the body of the uterus—the rarer variety	53	Still quite well—more than 7 years since the operation.
8	Mrs. S.	Cancer of body	June 8th, 1893	London Hospital; patient sent to me by Dr. Best, of Dover	Recovered	An example of "hard" cancer of the body of the uterus	57	Still remains quite well. Last examined at the London Hospital July 19th, 1900. No sign of recurrence.

No.	Name	Disease.	Date of operation.	Place.	Immediate result.	Remarks.	Age.	Remote result.
9	Mrs. M.	Cancer of cervix	July 20th, 1893	London Hospital	Recovered	—	35	Remained well till the autumn of 1894, *i. e.* for a little more than a year after operation, then recurrence took place. (Recurrence during the second year.)
10	Mrs. C.	Cancer of cervix	Aug. 4th, 1893	London Hospital	Recovered	—	38	Died with recurrence Feb. 23rd. 1895, 18 months after the operation. (Recurrence during the second year.)
11	Mrs. T.	Cancer of body	Aug. 21st, 1893	London Hospital	Recovered	Soft papillary growth. Perinæum had to be incised. After one side of uterus freed it was brought into the vagina by forceps like small midwifery forceps	54	Came up to the hospital and examined Nov., 1893, 3 months after operation. Quite well and no sign of recurrence. All efforts to trace her since failed, as she had left the former address.
12	Mrs. K.	Cancer of cervix	Aug. 28th, 1893	London Hospital	Recovered	Soft mushroom-like growth affecting both lips. I thought at the time of operation that the left broad ligament and left utero-sacral ligament were somewhat infiltrated, and that probably therefore removal of the uterus had not removed all the diseased tissue	42	She was seen and examined on Nov. 30th, 1893, when there was distinct evidence of recurrence in the top of the vagina. I think most probably that the whole of the cancerous tissue had not been removed by the hysterectomy. (Recurrence during the first year.)
13	Mrs. C.	Cancer of cervix	Feb. 1st, 1894	Private	Died	Deep laceration of cervix left side, with firm cicatricial band of tissue running from it. Impossible to draw uterus down properly. A large vessel, probably the uterine artery, retracted out of reach, and though it was ultimately secured, a fatal amount of blood had been lost before this could be done	48	—
14	Mrs. F.	Cancer of cervix	Feb. 22nd, 1894	London Hospital	Recovered	A case of large "cauliflower" growth	52	Recurrence took place in August, 1894. (Recurrence during the first year.)

15	Mrs. J.	Cancer of cervix	Feb. 27th, 1894	Private; with Dr. Howse, then of Barking Road, E., now of Reading	Recovered	An extensive "cauliflower" growth. It was not till the patient was under an anæsthetic that the operation seemed worth trying	57	This patient remained free from any sign of recurrence till she died in February, 1900. Dr. Howse saw her several times in her last illness. She died of phthisis.
16	Mrs. B.	Cancer of cervix	Aug. 13th, 1894	Private; sent to me by Sir J. Williams	Recovered	The case was an example of large "cauliflower" growth of the cervix, and there was a round nodule the size of a cobnut in the left broad ligament. As the uterus could be easily drawn down it seemed worth trying whether removal of the uterus and also of the nodule would be effectual	43	I believe recurrence took place not very long after the operation, but I had not the opportunity of examining the case after she left London. (Recurrence during the first year.)
17	Mrs. S.	Cancer of cervix	Aug. 16th, 1894	London Hospital	Recovered	An example of the nodular and infiltrating form of the disease, the whole cervix being much thickened by it. Little or no growth projecting from the vaginal portion. At the operation, though the uterus was removed, I felt sure some infiltrated tissue was left, especially at the base of the bladder	32	(Recurrence during the first year.)
18	Mrs. R.	Cancer of cervix	Aug. 30th, 1894	London Hospital	Died on 7th day of peritonitis	An example of a large "cauliflower" growth. This patient was doing quite well till the pressure forceps were removed at the end of the second day; while this was being done she complained of sudden severe pain, and within a few hours symptoms of peritonitis appeared. I believe in removing the forceps the general cavity of the peritoneum was reopened by breaking down adhesions, and so infection occurred. Since this case I always leave on the forceps at least three days, and often four.	39	—

No.	Name.	Disease.	Date of operation.	Place.	Immediate result.	Remarks.	Age.	Remote result.
19	Mrs. S.	Cancer of cervix	Oct. 13th, 1894	London Hospital; sent to me by Dr. Howse, then of Barking Road, E., now of Reading	Recovered	Cancer involving the substance of the cervix; little projecting growth. It is interesting to know that the patient had been told at another hospital that the case was too far advanced for operation to be advisable.	52	Has been seen at frequent intervals at the hospital since operation, and has remained quite well; last examined March 15th, 1900.
20	Mrs. N.	Cancer of cervix	Dec., 1894	London Hospital; sent to me by Dr. Winn, of Hackney	Recovered	The removal of the uterus probably did not remove all the tissue infiltrated by the malignant growth.	45	(Recurrence during the first year.)
21	Mrs.G.	Cancer of cervix	Feb. 14th, 1895	London Hospital; sent to me by Dr. Cory, of Bournemouth	Recovered	Large "cauliflower" growth.	26	Recurrence took place within a few weeks of the operation. (Recurrence during the first year.)
22	Mrs. de B.	Cancer of cervix	Apr. 25th, 1895	London Hospital; sent to me by Dr. Cursham Corner	Recovered	Large "cauliflower" growth, especially affecting the posterior lip of cervix. Was doubtful at time of operation if all infiltrated tissue was removed.	35	Seen and examined on several occasions, the last time on June 16th, 1898, when the scar was quite healthy, and no sign of recurrence anywhere. Heard that she went to America, and died either at the end of 1898 or early in 1899; no

								information as to cause of death. She was therefore known to be quite well over three years after operation, and if recurrence had been the cause of death it is very improbable that there should have been no sign of it on June 16th, 1898, if she died a few months after. It seems at least equally likely that she may have died from some independent cause.
23	Mrs. H.	Cancer of cervix	June 1st, 1895	Fitzroy House; sent to me by Dr. Garry Simpson, of Acton	Recovered	Large "cauliflower" growth, the part of the growth in the cervical canal just reaching internal os. There was a very large pyometra, the pus being horribly offensive	55	She has remained well since the operation. She has gone to Australia, but writes to me on each anniversary of her operation. The last letter, dated June 11th, 1900—five years after the operation,—says she was then quite well.
24	Mrs. H.	Cancer of body	Aug. 30th, 1895	London Hospital	Recovered	A large papillary growth projected into the cavity of the endometrium	48	Well, May 18th, 1897; also heard from her in May, 1900, that she was quite well.
25	Mrs. T.	Primary tubercular ulceration of cervix; believed at the time of operation to be cancer of the cervix	Jan. 30th, 1896	London Hospital; sent to me by Dr. Haslip and Dr. Howell	Recovered	—	36	Heard she was quite well, November, 1899, when I operated on a friend of hers.

No.	Name.	Disease.	Date of operation.	Place.	Immediate result.	Remarks.	Age.	Remote result.
26	Mrs. S.	Cancer of cervix	Apr. 16th, 1896	London Hospital; sent to me by Dr. Dunlop, of Aveley, Purfleet, Essex	Recovered	Large "cauliflower" growth of cervix	35	Seen and examined January 11th, 1899; a granular mass, size of raisin, at upper part of vagina. Seen recently, the mass is just the same, and evidently not malignant. She was quite well. Quite well March 15th, 1900.
27	Mrs. A. W.	Cancer of cervix	Sept. 7th, 1896	London Hospital	Recovered	Nodule of malignant growth size cob-nut or thereabouts, posterior lip; anterior lip appeared quite healthy. Supra-vaginal amputation done first, then on slitting up cervix the growth found to extend up to internal os, so body of uterus was then also removed	45	She was well up till about October, 1899, over three years since her operation. Then she began to fail, and came to the hospital in February, 1900, with a mass size of fœtal head in hypogastric region, fairly movable. Evident recurrence in the scar, and under the vaginal walls for some distance down. The glands in right groin much enlarged. She was looking cachectic; there was no projecting growth in region of scar, and only slight bleeding on examination. Very slight bleeding in October or November, 1899; for one day was the only spontaneous bleeding. (Recurrence during the fourth year.)
28	Mrs. I.	Cancer of body	Nov. 12th, 1896	London Hospital	Recovered	Secondary hæmorrhage in third week after operation requiring application of Wells's forceps. Subsequent incontinence of urine found on filling the bladder not to be due to any vesical fistula, but to a ureteral fistula. This persisted for some three or four months and then healed spontaneously	49	Recurrence in the recto-vaginal septum during the first half of 1900 (Recurrence during the fourth year.)

29	Mrs. W.	Sarcoma of body	Feb. 11th, 1897	London Hospital	Recovered	See 'Obstet. Trans.' for full report of case	24	Quite well March 24th, 1900.
30	Mrs. E. S.	Cancer of cervix	June, 1897	London Hospital	Recovered	—	About 60	Recurrence took place about a year after the operation. (Recurrence during the first year.)
31	Mrs. B.	Cancer of cervix	Aug., 1897	London Hospital; sent to me by Dr. Francis, of Leytonstone Road	Recovered	—	60	Recurrence took place and she died May 19th, 1898. (Recurrence during the first year.)
32	Mrs. B.	Cancer of body	Sept. 4th, 1897	Private; sent by Dr. Pope, of Kington, Hereford	Recovered	There were some mucous polypi attached to the lower part of cervix. The malignant growth was in the body	61	Last examined July 7th, 1900. No sign of recurrence.
33	Mrs. R.	Cancer of cervix	Sept. 6th, 1897	London Hospital	Recovered	—	38	Well June 21st, 1900.
34	Mrs. B.	Cancer of cervix	Sept. 23rd, 1897	London Hospital	Died three weeks after the operation of pneumonia	The only case I have had in which cancer of the cervix affected a procident uterus. This patient was mentally feeble and very difficult to manage after the operation. At the post-mortem the pneumonia was said to be not septic, and the parts in the neighbourhood of Douglas's pouch were looking healthy	53	—
35	Mrs. H.	Cancer of cervix	Oct. 5th, 1897	Private; with Dr. McMullen, of Brixton	Recovered	A rather advanced case	52	Died of recurrence July, 1898, the scar remaining unaffected to the last. (Recurrence during the first year.)

No.	Name.	Disease.	Date of operation.	Place.	Immediate result.	Remarks.	Age.	Remote result.
36	Mrs. E. M.	Cancer of cervix	Dec. 2nd, 1897	London Hospital; sent to me by Dr. Honnywill, of Sutton	Recovered	—	46	Examined and found quite well March 22nd, 1900, more than three years since the operation.
37	Mrs. D.	Cancer of cervix	May 12th, 1898	London Hospital; sent to me by Dr. Jackson, of King's Lynn	Recovered	A rather advanced case with large conical ulcer	38	Recurrence took place March, 1899. She became much worse June 5th, 1899, and died soon after. (Recurrence during the first year.)
38	Mrs. S.	Cancer of body	May 14th, 1898	Fitzroy House; Dr. Johnston, of Maidstone	Recovered	—	About 50	—
39	Mrs. R.	Cancer of cervix	Feb. 16th, 1899	London Hospital	Recovered	Bleeding on taking off forceps, requiring application of one pair more for another two days	36	Quite well July 26th, 1900.
40	Mrs. E. K.	Cancer of cervix	April 27th, 1899	London Hospital	Recovered	The disease affected both the vaginal and supra-vaginal portions of the cervix	36	Recurrence early in 1900. (Recurrence during first year.)

TABLE II.—*Twelve Cases of Vaginal Hysterectomy for Cancer of the Uterus in which the Disease is known not to have recurred.*

No.	No. in Table I,—a consecutive series of 40 vaginal Hysterectomies for cancer.	Disease.	Date of operation.	Place of operation.	Interval since operation without recurrence.	Microscopic characters of growth.
1	7. Mrs. D.	Cancer of body	Feb. 1st, 1893	Private; with Dr. Stott, of Highgate Road, and Dr. Godson	7 years and 4 months. I saw her on 18th of June, 1900	Extract from Clinical Research Association's Report (Mr. Targett):—"The growth may be described as a villous carcinoma."
2	8. Mrs. S.	Cancer of body	June 8th, 1893	London Hospital; sent to me by Dr. Best, of Dover	7 years. Examined July 19th, 1900, at the London Hospital. No recurrence	Extract from Clinical Research Association's Report (Mr. Targett):—"A soft columnar-celled carcinoma."
3	15. Mrs. J.	Cancer of cervix, large "cauliflower"	Feb. 27th, 1894	Private; with Dr. Howse, then of Barking Rd., E., now of Reading	6 years	Extract from Clinical Research Association's Report (Mr. Targett):—"The nature of the growth is undoubtedly squamous-celled epithelioma."
4	19. Mrs. S.	Cancer of cervix	Oct. 13th, 1894	London Hospital	5½ years (up to March 15th, 1900, when the patient was last examined)	Extract from Clinical Research Association's Report (Mr. Targett):—"The substance of the cervix is infiltrated with branching processes of squamous-celled epithelioma."
5	23. Mrs. H.	Cancer of cervix, large "cauliflower." Pyometra	June 1st, 1895	Private; sent to me by Dr. Garry Simpson, of Acton	5 years. Heard from her in letter dated June 11th, 1900, that she was quite well	Extract from Clinical Research Association's Report (Mr. Targett):—"Solid branching columns of squamous-celled epithelioma are shown infiltrating the substance of the cervix uteri."
6	24. Mrs. H.	Cancer of body	Aug. 30th, 1895	London Hospital	4¾ years (up to May, 1900, when I heard from her that she was quite well)	Extract from Clinical Research Association's Report (Mr. Targett):—"The growth from the body of the uterus is a soft, glandular-celled carcinoma, which has extensively infiltrated the muscular substance."

No.	No. in Table I,—a consecutive series of 40 vaginal hysterectomies for cancer.	Disease.	Date of operation.	Place of operation.	Interval since operation without recurrence.	Microscopic characters of growth.
7	26. Mrs. S.	Cancer of cervix	April 16th, 1896	London Hospital; sent to me by Dr. Dunlop, of Purfleet	Nearly 4 years. I saw her on March 15th, 1900, and she was quite well	Extract from Clinical Research Association's Report (Mr. Targett):—"This portion of the cervix uteri is thickly infiltrated with a soft squamous-celled epithelioma."
8	29. Mrs. W.	Sarcoma of body, "deciduoma malignum"	Feb. 11th, 1897	London Hospital	More than 3 years (up to March 24th, 1900, when I last examined her)	For full report of this case see Lond. 'Obst. Soc. Trans.,' vol. xxxix, for 1897, p. 246.
9	32. Mrs. B.	Carcinoma of body	Sept. 4th, 1897	Private; with Dr. Pope, of Kington, Hereford	2 years and 10 months (up to July 7th, 1900, when I last examined her)	Extract from Clinical Research Association's Report (Mr. Targett):—"The tissue from the body of the uterus is extensively infiltrated with a soft columnar-celled carcinoma."
10	33. Mrs. R.	Cancer of cervix	Sept. 6th, 1897	London Hospital	2 years and 9 months (up to June 21st, 1900, when I last examined her)	Extract from Clinical Research Association's Report (Mr. Targett):—"The substance of the cervix uteri is extensively invaded with thick branching processes of squamous-celled epithelioma."
11	36. Mrs. E.M.	Cancer of cervix	Dec. 2nd, 1897	London Hospital	2 years and nearly 4 months (up to March 22nd, 1900, when I last saw her)	Extract from Clinical Research Association's Report (Mr. Targett):—"The growth in the cervix uteri is a malignant adenoma,—that is, a columnar-celled carcinoma in which the cells preserve their tubular arrangement."
12	39. Mrs. R.	Cancer of cervix	Feb. 16th, 1899	London Hospital	1 year and 5 months (up to July 26th, 1900, when I last examined her)	Extract from Clinical Research Association's Report (Mr. Targett):—"The cervix is very extensively invaded with squamous-celled epithelioma. Some of the epithelial processes are large, and the central cells have undergone granular degeneration. In others there are small cell-nests."

DISCUSSION.

Professor BRIGGS (Liverpool).—The results of the operation of vaginal hysterectomy produced this evening by the author of the paper would tend to establish the position of the operation much more than, for instance, my own. Since March 24th, 1889, up to the present I have operated on 83 cases of malignant disease of the uterus (4 deaths). Of the 83 growths 3 were sarcomata of the cervix, 65 carcinomata of the cervix, and 15 carcinomata of the body of the uterus. To adopt Dr. Lewers's date limit, up to the end of April, 1899, I have 57 cases to report upon, and amongst them the deaths from operation were 3, including 1 from embolic septic pneumonia on the thirty-fifth day. Of the 57, 10 were cases of corporeal cancer, showing 5 patients apparently cured, and 46 were cases of cervical cancer. Of these my reports at present are incomplete, but in 5 cases complete cures are apparently promised. Adding to these the 1 case of cervical sarcoma operated upon over ten years ago, there are perhaps only 11 out of 57 patients completely cured by operation. Delay in diagnosis has always to be remarked upon, and if patients object to examination use could be made of the ordinary medico-legal tests for blood in the intermenstrual discharges. I have brought with me water-colour drawings, from which you will gather that many of my cases were in a more advanced stage than Dr. Lewers's; but I intend to complete my clinical reports in the near future, and on one or two occasions in the past I have been gratified to find the results better than I had anticipated, owing to broad ligament indurations not having proved malignant. Recently my assistants and I have analysed 100 malignant growths of the uterus in the laboratory of University College, Liverpool; 74 were carcinomata, 6 sarcomata, and 20 malignant adenomata. Amongst the 83 included in my series of operations already referred to, I may mention that the cases of malignant adenoma were 4 of the cervix and 11 of the body of the uterus. The cases of malignant adenoma have proved more amenable to radical treatment. I have adopted similar methods to those of Dr. Lewers in diagnosis and in operating. I desire to congratulate Dr. Lewers on results which at present seem to be better than my own. Amongst even advanced cases of corporeal cancer the proportion of cures is high, but amongst the cervical carcinomata cures have rarely been obtained. It is amongst the latter that Dr. Lewers's results are so strikingly good when compared with my present acquaintance with my own.

Dr. A. ROUTH.—Those who know how difficult it is to follow

up hospital cases will realise how indefatigable the author must have been to obtain the histories up to date. I also have done 41 cases of vaginal hysterectomy, 15 being of the body and 26 of the cervix. That seems a large proportion of cases in which the body was affected, resembling in this respect the author's figures, he having had 11 out of 40. I imagine the reason why one gets a larger proportion of cases of cancer of the body of the uterus is that they come earlier under observation. The history in such cases of cancer of the body is usually that there has been a period of amenorrhœa after the menopause, and that then hæmorrhage comes on which attracts attention, and this leads to an examination being made, whereas the disease at an early stage in the cervix may escape notice for a time. Moreover pain is a much more marked symptom in cancer of the body. This is also probably one reason why recurrence does not take place so often in cancer of the body. My mortality was also three. One, on the sixth day, was a case of cancer of the cervix in an alcoholic patient who died of exhaustion, and two of cancer of the body, both dying suddenly when I thought they were convalescent, one on the sixteenth day and the other on the twenty-fourth day, acute mania having developed on the sixteenth day. One of the cases of cancer of the body was a malignant papilloma, and two malignant adenoma with one sarcoma, removed by the vagino-abdominal method. The cases of cancer of the body did not as a rule recur as early as in cancer of the cervix. One patient is alive two and a quarter years after the operation, one three years and a half, another four years after. Of twenty-six cases of cancer of the cervix with one death, recurrence was less satisfactory. Four or five cases recurred within a year, one two years after, another three years after, and one, a very disappointing one, seven years after. I saw this latter patient every six months, and I thought she had permanently recovered. Recurrence took place in the cicatrix and she soon died. One patient operated on in 1892 and another in 1895 are still free from recurrence. From the figures brought forward to-night it is evident that the opinion expressed by some that this operation is useless cannot be true. I am surprised that the author uses forceps for his broad ligaments. He began with using ligatures and finished with forceps, whereas I began with clamps and turned to ligatures. It seems to me more surgical to use ligatures than forceps, as the latter leaves a large slough to come away, the temperature is higher, and the discharge very offensive. If I have to use forceps I generally leave them on thirty-six hours. Like the author, I never attempt to operate if I find that the uterus has indurations in the broad ligament, or if the utero-sacral folds or bladder are implicated. If in

doubt I get permission to do the operation if possible, and after drawing the uterus down I open Douglas's pouch first, instead of making an anterior incision and separating the bladder, which is usually the first step. I then pass the finger into Douglas's pouch, and am able to accurately estimate whether the disease has spread into surrounding tissues. If it has I prefer not to remove the uterus. How long does the author keep the gauze in? At first I took it out in two or three days, but I find now that I get better results if I leave it in seven or eight days. Of 15 cases of vaginal hysterectomy for cancer of the body two died (sixteenth and twenty-fourth day) suddenly. Of the others two recurred within one year, two within two years, and one in three years. Of those who are still alive without recurrence after two years from the operation, one has lived six and a half years, one four and a quarter, and two two and a half years. Of 26 cases of cancer of the cervix one died on the sixth day (chronic alcoholism). Of the others six recurred within one year, three within two years, and one after six and a quarter years. Of those who have survived more than two years and are now without recurrence, one has lived five years, two over four years, three over three years, and two over two years.

Mr. Bowreman Jessett.—I have published 107 cases in the 'British Gynæcological Journal' of hysterectomy for cancer, and have now performed the operation in over 150 cases. My conclusions support those advanced by the author, viz. that a very fair percentage of cases of carcinoma of the uterus, if seen in an early stage, can be what may practically be called cured, *i.e.* patients are relieved from their sufferings for a period of from three to nine years. The whole gist of the author's paper is early diagnosis, and I am quite sure that this is the practical conclusion of any one who has had much experience of these cases. Patients go about a long time with purulent or sanguineous discharges without consulting a doctor, or the doctor contents himself with prescribing some astringent lotions, etc. Many patients object to being examined, but I contend that it is the duty of the medical man, to himself and to his patient, to insist upon a thorough examination in all cases where there is any abnormality of the uterine secretions, especially in women at or after the menopause. If such an examination were made the disease would be recognised at a much earlier stage than is often done at present, and if treated surgically such patients would stand a very much better chance of obtaining relief. The operation is not of itself dangerous, the mortality being at the outside from 5 to 8 per cent. Some people say vaginal hysterectomy is a very simple and easy operation, but though I have seen some very simple operations where the

uterus could be drawn completely outside the vulva, and the fornices readily opened, I have also seen others of extreme difficulty. The difficulty in many cases of getting the uterus down is very great. I have in nearly every instance used ligatures for securing the vessels, which seems to me a far more surgical procedure than adopting forceps for the same purpose. The only mishap I have ever had was after using forceps. The principal difficulties are that you often get adhesions of the uterus in Douglas's pouch to the rectum, the sigmoid flexure, or small intestine, and these adhesions are very difficult in many cases to separate. In one case in which I used forceps there were very strong adhesions to the upper part of the rectum, and I had some difficulty in catching up the ovarian artery. Everything went well for ten days, when a large slough came away and a recto-vaginal fistula formed. I endeavoured to close this later, and found it quite at the top of the vagina, and it was next to impossible to do so. Another danger is that of tearing into the bladder, which happened to me in one case which appeared on examination to be one of the simplest of cases, but on opening the anterior fornix I found that the disease had extended from the cervical canal into the cellular tissue and had infiltrated the bladder, and in trying to separate it the bladder was torn and a fistula formed which caused much trouble later. The ureters are also much more likely to be injured by forceps than by the ligatures. I would ask the author whether he employs Doyen's plan of splitting the anterior wall of the uterus and drawing it down. In cases of a very large uterus I always employ that procedure, as it undoubtedly facilitates matters materially. The author has not alluded to the malignant degeneration of fibroids, and I should like to know his experience thereof. Such cases are in my experience the most favourable for operation. I cannot agree with Dr. Routh that cancers of the body of the uterus are the earliest met with and the easiest to diagnose. I think these are very difficult to recognise; indeed, I cannot suggest any way of doing so for certain in the early stages, excepting by anæsthetising the patient, dilating the uterus, and curetting and examining the fragments microscopically. Even in some of these cases pathologists have reported that there was no malignancy, yet they have proved to be malignant, a small growth being found in the fundus which might escape the curette or not be included in the scraping submitted to the pathologist for examination, thus showing how difficult these cases are to diagnose in the early stage. Then as to hæmorrhage being one of the early symptoms after the menopause: that is true, but there is often a still earlier symptom, and that is slight hæmorrhage after coitus, which in my experience is not uncommon. In the post-mortem

room I have been struck by the very small number of cases in which the sacral and iliac glands are involved, and this induced me to urge patients to submit to hysterectomy. I would point out that the treatment of the peritoneal flaps is rather an important point. They have a tendency to curl up after division, and if you do not take the trouble to pull these flaps down you may get an accumulation of blood-clot which may give rise to trouble. I make a point of drawing both flaps well down. Personally I do not withdraw the gauze for five, seven, or even ten days.

Mr. CHARLES RYALL.—As to the frequency with which recurrence takes place in epithelioma of the cervix in contradistinction with that of the body of the uterus, we all know how easy it is to transplant malignant disease in a patient already suffering therefrom. It has struck me that at the time of the operation we are very likely to infect the wound. In carcinoma of the fundus the disease is surrounded by a certain amount of healthy tissue, which is not the case in the cervix. Pieces of the growth may be broken off and left in the wound, thus leading to recurrence. The author's large percentage of recoveries may be accounted for by the use of the actual cautery, which is a strong antiseptic. This danger of infection was very strongly brought before me not long since in a case of cancer of the fundus, for which *abdominal* hysterectomy was performed. During the operation I tore the uterus across at the internal os, so that the fundus had to be removed first. A year later that patient came with recurrence in the vaginal *cul-de-sac* causing pressure on the rectum. She also had a swelling in the abdominal scar the size of a large walnut. Colotomy was done, and I took advantage of the opportunity to examine the peritoneal scar, and there were no adhesions at all. I removed a piece of the growth in the scar, and it was found to be identical with the original growth in the uterus of a year before. I agree with Mr. Jessett that Doyen's method is of great assistance when the uterus is large. As to palliative cases, the author goes perhaps a little too far. He gives us 27 per cent. of cures, so that the other 71 per cent. can only have been palliative operations. In cases of cancer of the uterus which cannot all be got away, if an operation only rids the woman of the foul discharge for six months, it is only fair to give her the benefit of it, without thinking only of our statistics.

Dr. WALTER TATE.—In eleven of Dr. Lewers's cases of cancer of the body of the uterus there was freedom from recurrence in five, or about 50 per cent., and in twenty-eight of cancer of the cervix there was freedom in 25 per cent. That corresponds to the results obtained by most operators. I have myself operated on upwards of seventy cases by vaginal hysterectomy for cancer

of the cervix and body, but I do not agree with the author in looking upon this operation as only suitable for cases in which the disease is definitely localised in the uterus. So far as I have seen, cases in which there is a slight amount of thickening in the broad or utero-sacral ligaments, in which patients suffer from discharges and severe hæmorrhages, may be very greatly relieved by removing the uterus, provided the thickening is slight and not sufficient to interfere with the uterus being brought down near the vulva. Dr. Martin, of Berlin, made the remark some years ago that where vaginal hysterectomy is an easy operation it is a good operation, and where it is difficult it is a bad operation. In some of these cases where there has been thickening of the broad ligament the freedom from recurrence has been much longer than in cases in which *a priori* the prospect was much more favourable; therefore the operation is desirable and justifiable as a palliative measure even when to all appearance it is not likely to be permanently curative. I have lost five cases out of the seventy, but only two out of the last fifty.

Dr. CHAMPNEYS.—The author's statistics quite negative the view that vaginal hysterectomy is an operation which should not be performed, or which is of no use. Of course cancer is altogether a very disappointing disease, and even when the prognosis before operation seems excellent we must expect a great many disappointments. I have not my figures with me to-night, but I have several patients going about apparently quite well several years after operation. The author did not allude to one of the most valuable forms of examination, viz. *per rectum*. This enables us to reach much higher than *per vaginam*, and you can feel the back of the uterus and the utero-sacral ligaments. Like him I began with ligature, and have finally adopted the forceps, but I do not use Wells's forceps, because the serrations seem to me to be in a wrong direction; they are transverse, which is parallel to the direction of the vessels; so I have mine made with diagonal serrations. With regard to the operation in advanced disease I agree with what he has said. If the disease has gone beyond the uterus I do not think the operation should be done. In many cases it is very difficult to make out whether it has or not. There may be some induration or want of elasticity in one or other broad ligament, and one cannot know beforehand whether it is due to inflammation or to malignant infiltration. Very often in such cases anæsthesia will clear up the doubt, for the induration may become plastic, so to speak, and there is an absence of nodules; in such cases I give the patient the benefit of the doubt. The difficulty and danger of the operation is certainly very much enhanced when the broad ligament is involved. I should like to know what

evidence Mr. Jessett has of fibroids undergoing malignant degeneration. That fibroids may coincide with malignant disease merely shows that a woman with fibroids is not protected against the common fate. It must of necessity be very difficult to prove that an innocent growth takes on malignant degeneration, and I have only met with one case in which I suspected that this might have been the case.

Dr. HERBERT SPENCER.—I cannot speak too highly of the truly admirable way in which the author has tabulated and arranged his cases. I am particularly interested in the instance of implantation mentioned by Mr. Ryall. Many examples of this cancer-implantation ("Impfmetastase") are on record. In order to prevent its occurrence I have usually performed high amputation in cancer of the cervix instead of vaginal hysterectomy, the operation being performed of late years entirely by the actual cautery with extremely good results. I have not lost a case in thirteen years. It is an idea I owe to Dr. Byrne, who in some 400 cases has only had one death. It is practically a safe operation. I believe that the improvement in this operation will lie in the fact of using the cautery for the removal of the cervix or uterus. I have used it for the removal of the whole uterus *per vaginam*. With modern improvements in cautery forceps I think we shall be able to remove the uterus with a very small mortality, and that the searing of the tissues prevents the implantation of cancer on the raw surfaces. It is remarkable that Jacobs, of Brussels, with a very large experience, has not had one case survive for two years. Most foreign operators cut up the uterus with knife or scissors, but this, I think, ought not to be done in cancer. It is especially in fibroids that it renders excellent service, but in cancer the less we cut up the better. I have a number of cases remaining well five years or more after operation. I cannot to-night give figures, but I am convinced that the use of the cautery is an extremely valuable method of operating.

Dr. LEWERS.—I could not follow Dr. Briggs's figures, but I hope he will publish his cases in a form we can refer to. I must congratulate Dr. Routh on his low mortality, which is the same as my own. I should think we get cases of malignant disease of the body more frequently in an earlier stage than cases of cancer of the cervix. It is difficult to account for this so far as the examination of the case goes, for a well-marked projecting growth on the vaginal cervix is much more easily recognised by the doctor examining than a malignant growth in the body of the uterus, which can only be recognised by dilating the cervix. My own belief is that in cases of cancer of the cervix and probably of the body there are no symptoms at all in the early stages. It is not a question which is the earlier

symptom, but I believe there is a stage in which the growth can be recognised by local examination at a time when there are no symptoms. I remember the case of a patient from whom I removed a fibroid polypus projecting through the cervix; she was of a nervous temperament, and she came at intervals afterwards to see that she was all right. On one occasion there was a well-marked raised patch on the anterior lip of the cervix, not the spot where the polypus was attached, and I felt convinced that it was malignant. Sir John Williams took the same view, and the case was operated on; the growth was found to be malignant. At that time the patient complained of nothing whatever—no hæmorrhage, either after coitus or at other times, and she had no discharge. Therefore we may take it that in the early stages there may be no symptoms, and that is one reason why we get these cases as a rule so late. A case of recurrence after seven years, such as that mentioned by Dr. Routh, is particularly disappointing. I may repeat what I have said in my paper that these cases do not include all my cases of operation for cancer. Many of my earlier cases were operated upon by high amputation of the cervix, and some of my best cases, as regards the after results, belong to that series; possibly because, being the first cases, they have had longer to run. In December, 1892, I read a paper before this Society comprising a number of these cases; among that series I can say positively that there are two patients, one thirteen and one twelve years after operation, who are now perfectly well. In regard to forceps *versus* ligatures, I confess that I should like to use ligatures. I used them in the first three cases. They are much more comfortable for the patient, and the use of the forceps entails much discomfort; but as a rule I have been well satisfied with forceps. My experience of ligatures is that it is extremely difficult to apply them in such a way as to secure us against hæmorrhage. The uterus is drawn down and the parts are put on the stretch, and I have seen cases where, when the operation was supposed to be over, the ligatures slipped off with profuse hæmorrhage, and it has been necessary to use the forceps after all. I, too, have altered the serration of the forceps, and use a pattern with oblique grooves as mentioned by Dr. Champneys. I generally leave the gauze in for four days,—in fact, until I take out the forceps. With ligatures it is quite a different matter, and it then may be good practice to leave it in longer. You cannot do this if you use forceps, because they cannot be removed easily with the gauze in position. In reference to the formation of a fæcal fistula, it often happens that a piece of intestine is infiltrated, and possibly that might have been so in Mr. Jessett's case. I agree with Dr. Champneys that it is important to preserve the integrity of the specimen, because you

lose the outline of the malignant growth if you cut it up, and may easily leave some of it behind. With regard to cancer of the body of the uterus, by the time the uterus is so large as to offer an obstacle to removal by the vaginal route, it is usually beyond the reach of surgical aid. In such cases it is best to do abdominal hysterectomy, which seems to me better than splitting the uterus. I know nothing at all about fibroids becoming malignant. I have been looking out for such cases for years, and I cannot recall a single instance in which I have satisfied myself that such has been the case; for the present, therefore, I remain sceptical. Some Continental observers assert that the glands are always affected in all the cases of cancer of the cervix that come to us, but my results, I think, show conclusively that this cannot be the case. I approve of the idea of drawing down the peritoneal flaps, and shall bear Mr. Jessett's remarks in mind. I decline to admit that it can be right to perform vaginal hysterectomy on advanced cases of cancer when there is no prospect whatever of permanent relief. Unless we are going to get something better than a few months of comparative comfort I really do not think it is worth while. Recurrence usually takes place in the scar and quite exceptionally in the glands, so that it is rare for the patient to be relieved from the misery of a constant discharge. I myself never do vaginal hysterectomy as a palliative measure. It is true that many of my operations proved to be nothing more, but I did not operate with that object in view. I have never removed the uterus entirely by the cautery, as mentioned by Dr. Spencer, but I shall be prepared to try it.

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No. 7. (Table I.)

Cancer of body of uterus. Vaginal Hysterectomy, February 1st, 1893. The patient was seen on June 18th, 1900, and expressed herself as feeling quite well.

A.—Peritoneum. **B.**—Cut surface of uterine wall. **C.**—Growth in endometrium (villous carcinoma). **D.**—Cervical canal.

No. 7. (Table I.)

Fig. A depicts the general characters of this growth under a low power. In the muscular tissue of the uterus there are spaces of various sizes from simple gland-like tubules to cysts visible to the naked eye, and filled with a complicated epithelial new growth. This growth has resulted from proliferation of the columnar epithelium lining the tubules, and has assumed in part the form of intra-cystic villous papillomata. At the periphery of the largest space the malignancy of the growth is shown by extension of solid processes into the adjacent uterine tissue. (Mr. Targett's description for the Clinical Research Association.)

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In Fig. B (high power) two of these intracystic papillomata are represented. In the vascularity and delicacy of their structure they closely correspond with the fimbriated papilloma of the urinary bladder. The growth may be described as a villous carcinoma. (Mr. Targett's description for the Clinical Research Association.)

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No. 8. (Table I.)

Primary carcinoma of the body of the uterus. Vaginal Hysterectomy, June 8th, 1893. The patient was seen and examined at the London Hospital on July 19th, 1900, and found to have no sign of recurrence.

A.—Peritoneum. **B.**—Cut surface of uterine wall. **C.**—Growth in endometrium "a soft columnar-celled carcinoma." **D.**—Cervical canal.

No. 8. (Table I.)

Fig. A (low power) represents a portion of uterine wall composed of interlacing bundles of muscular tissue, and extensively infiltrated by a soft columnar-celled carcinoma. The cells are arranged in tubules and elongated spaces, which have a definite lumen, and the stroma consisting of uterine muscle is very scanty. (Mr. Targett's description for the Clinical Research Association.)

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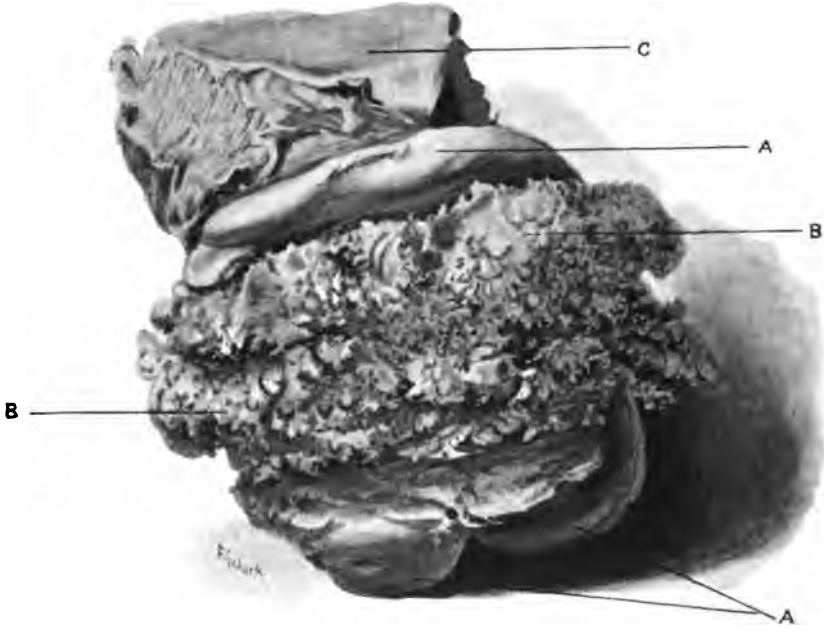
In Fig. B (high power) the columnar character of the cells is shown, and although the tubules and alveoli everywhere exhibit a central cavity or lumen, yet there are abundant signs of epithelial proliferation, and the cells encroach on the central space. In the well-marked tubular structure of the growth, this specimen resembles the so-called malignant adenoma. (Mr. Targett's description for the Clinical Research Association.



No. 15. (Table I.)

Vaginal Hysterectomy, February 27th, 1894. No return six years after the operation, when the patient died of phthisis.

A.—Epithelial surface of vaginal portion of cervix.
B.—Growth "squamous-celled epithelioma."
C.—Portion of peritoneum on body of uterus.

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No. 19. (Table 1.)

Fig. A (low power) shows epithelial alveoli of varying size and shape, which are invading the muscular substance of the uterus. The cells are arranged in a single row of columnar epithelium at the periphery, and towards the centre they become much more irregular and compressed. A few cell-nests are seen, and they are numerous throughout the section. (Mr. Targett's description for the Clinical Research Association.)

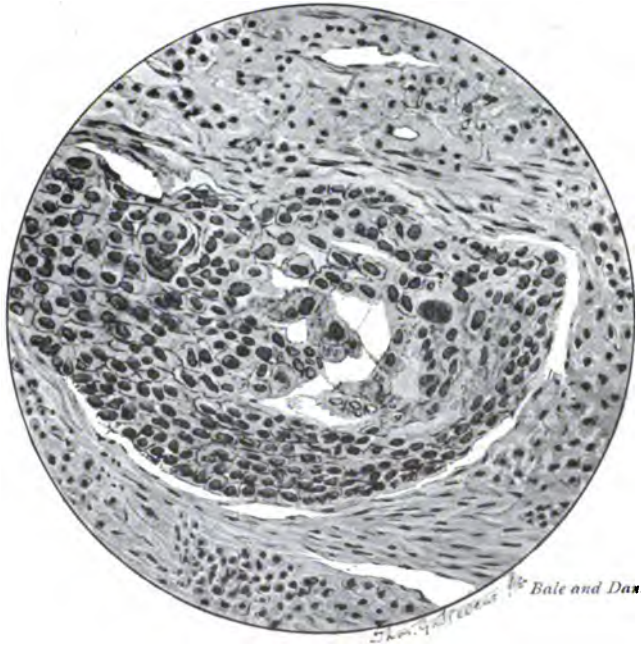

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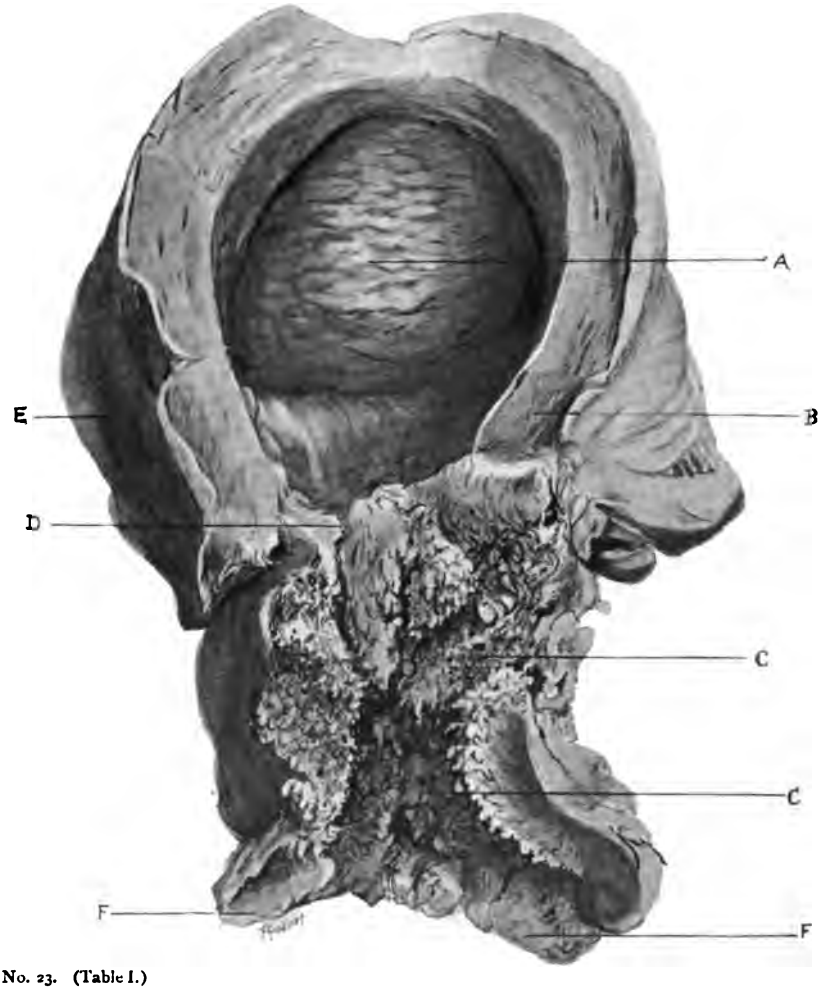
Fig. B (high power). In this sketch one alveolus is represented made up of typical squamous epithelial cells. To the left a whorl of cells is seen in process of formation of a cell-nest. The vessels in the adjacent uterine substance are dilated. (Mr. Targett's description for the Clinical Research Association.)



No. 23. (Table I.)

Vaginal Hysterectomy, June 1st, 1895. I heard from the patient (who is in Australia) in a letter dated June 11th, 1900, that she was quite well.

A.—Cavity of body of uterus enormously dilated. It contained fœtid pus (pyometra) which escaped during the operation.
B.—Cut surface of wall of body of uterus.
C.—Growth in cervix, "squamous-celled epithelioma."
D.—Internal os.
E.—Peritoneal surface of uterus.
F.—External os.

No. 23. (Table I.)

Fig. A (low power). Solid Branching columns of squamous-celled epithelioma are shown infiltrating the substance of the cervix uteri. Large cell-nests are present, as well as areas of granular degeneration in the centres of the epithelial processes. (Mr. Targett's description for the Clinical Research Association.)

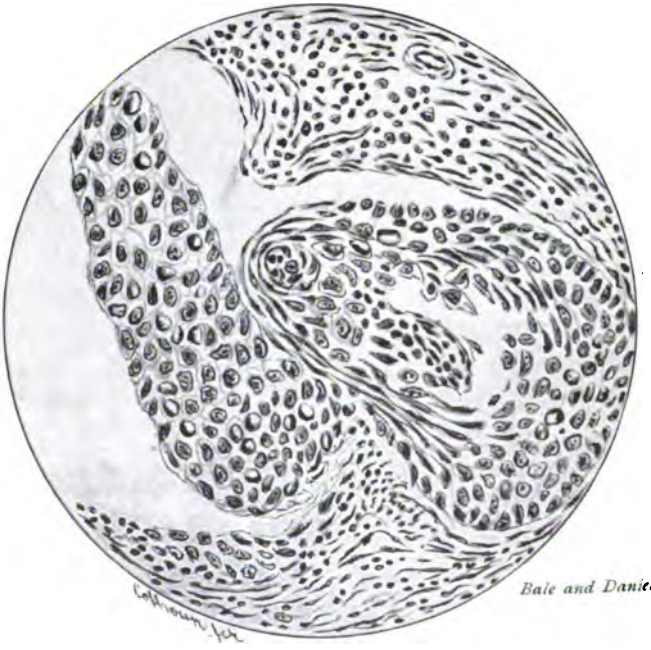


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Fig. B (high power). The squamous character of the epithelial cells is here represented, and in the centre keratoid and other degenerative changes have taken place. The cells have separated from the stroma by shrinkage. (Mr. Targett's description for the Clinical Research Association.)

No. 24. (Table I.)

In Fig. A (low power) is represented a soft glandular-celled carcinoma invading the body of the uterus. The cells are arranged in elongated alveoli, and a strand of muscle tissue crosses the section. At the highest point in the field the growth has undergone granular degeneration and necrosis. (Mr. Targett's description for the Clinical Research Association.)

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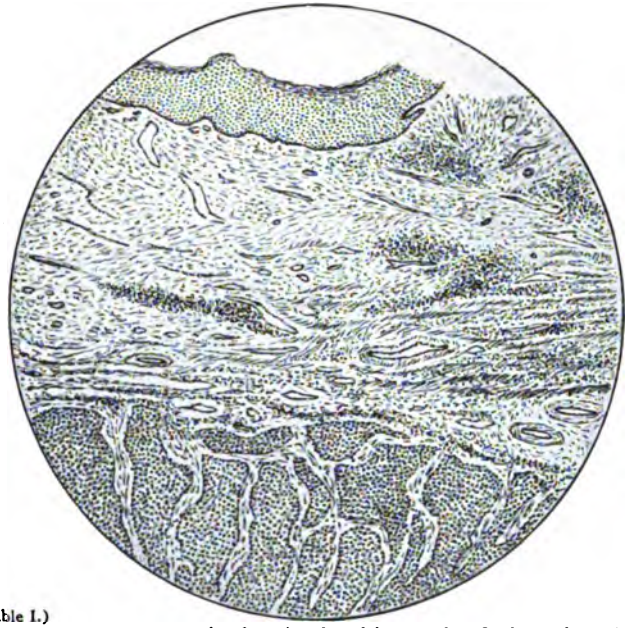
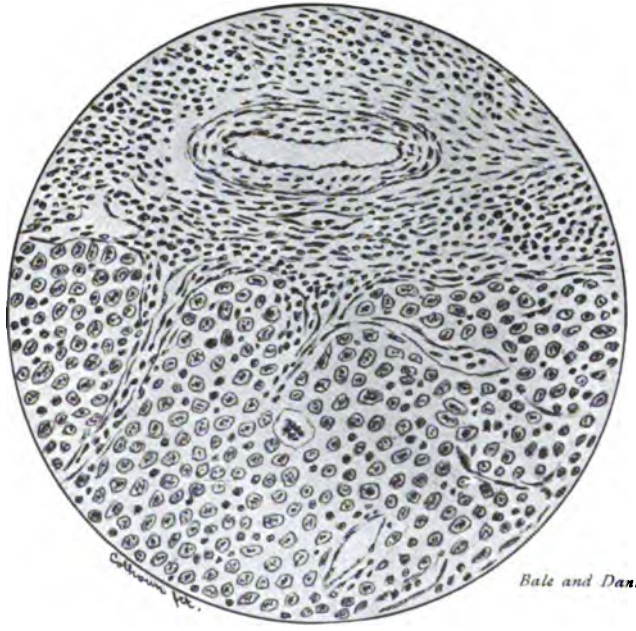
In Fig. B (high power) the cells are seen to be of moderate size and fairly uniform shape. There is no indication of a tubular arrangement, and the small round nuclei indicate leucocytes invading the degenerate areas. (Mr. Targett's description for the Clinical Research Association.)



No. 26. (Table I.)

Fig. A represents a low power view from the edge of the growth. In the cervix uteri, at the top, is a portion of vaginal mucous membrane, and beneath this comes a broad strand of submucous tissue and bundles of unstriped muscle. The vessels are distended, and many foci of small round inflammatory cells are seen in this layer. At the bottom of the field are depicted the solid elongated processes of the squamous-celled epithelioma. (Mr. Targett's description for the Clinical Research Association.)



In Fig. B a portion of the growth under a higher power is represented. The cells are large, but their outlines are very indistinct, so that merely their large round or oval nuclei with nucleoli are recognisable. No cell-nests are present, but a few larger cells may be seen which exhibit the so-called "cell-inclusions." One of these is represented in the drawing. The stroma consists of a few strands of cellular tissue in which the vessels run. (Mr. Targett's description for the Clinical Research Association.)

MEDIAN PERINEAL URETHROTOMY AND CYSTOTOMY

THROUGH A SUPERFICIAL TRANSVERSE INCISION, AFTER CELSUS

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In some special cases I have found it advantageous to reach the neck of the bladder by first making a superficial semilunar incision across the perineum, and then a second deep one exactly along the middle line, so as to lay open the hinder part of the urethra and the neck of the bladder.

I do not regard the method as supplanting the well-known supra-pubic and perineal operations, except lateral lithotomy, which has rightly lapsed into disuse, but as applicable to certain special cases, such as are detailed below.

There is nothing novel in the procedure; on the contrary, it is the earliest of all systematically described lithotomy operations, viz. that given by Celsus,[1] book vii,

[1] Celsus, having described the holding of the patient in the lithotomy position by assistants, and the bringing down of the stone to the neck of the

chap. xxvi. It has been used for perineal prostatectomy, and is described and figured by Kocher ('Text-book of Operative Surgery,' by Dr. Theodor Kocher, translated from the second German edition by Mr. H. J. Stiles, pp. 163—165, figs. 74 and 75), where it is said to have been practised by Dittel and Zuckerkandl. I am fully aware that this operation described by Celsus has not been largely followed, and that by suggested emendations of the text and strained commentaries it has been sought to explain the passage as an obscure description of left lateral lithotomy. I am only concerned to show that, taking the description of Celsus as it stands, his operation agrees essentially with that which I have carried out. The anus was held out of the way by

bladder by the index and middle finger of the left hand in the rectum, whilst the fingers of the right hand made pressure on the hypogastrium, says, "Over the neck of the bladder near the anus a lunate incision, the horns of which point a little towards the hips, is cut through the skin as far as the cervix of the bladder; then, below the skin, a second incision is to be made, crossing the first where it is convex, which lays open the cervix until the urethra is exposed, and so that the wound is a little larger than the calculus." The calculus then comes into view, and may be pushed out or extracted by the fingers or by a special scoop, against which, if too large, the stone may be broken by a chisel. Celsus continues, "For those who, for fear of a fistula, which in this position the Greeks call korusda, make too small an opening, are afterwards brought to this very result with still greater danger; for the calculus makes a way for itself, when forced out, unless it find one. It is even more dangerous still when the shape of the stone or its rough surface contributes to this effect, from which both hæmorrhage and over-stretching of nerves may be produced, which if any one escapes, yet he will have a larger fistula by the cervix being torn *than he will if it be cut.*"

"Cum jam eo venit, incidi super vesicæ cervicem juxta anum cutis plaga lunata usque ad cervicem vesicæ debet, cornibus ad coxas spectantibus paulum: deinde ea parte, qua resima plaga est, etiamnum subcute altera transversa plaga facienda est, qua cervix aperiatur, donec urinæ iter pateat sic, ut plaga paulo major, quam calculus sit.—Nam, qui metu fistulæ (quam illo loco κορυάδα Græci vocant) parum patefaciunt, cum majore periculo eodem revolvuntur: quia calculus iter, cum vi promitur, facit, nisi accipit: idque etiam perniciosus est, si figura quoque calculi, vel aspritudo aliquid eo sontulit. Ex quo et sanguinis profusio, et distentio nervorum fieri potest: quæ si quis evasit, multo tamen patentiorum fistulam habiturus est rupta cervice, quam habuisset, incisa."

the fingers of the left hand, which drew the stone towards the perineum; a free superficial incision was made, and then by a deep median incision the neck of the bladder was *divided*, not ruptured, sufficiently to allow of the removal of the stone without the production of complications and of a urinary fistula.

The operation, as I have performed it, is as follows:— The patient, prepared by shaving and cleaning, is placed in the lithotomy position with the pelvis raised by a sand-bag. The central point of the perineum is then made the middle of a horseshoe-shaped incision of the skin, the ends of which terminate on either side of the anus just internal to the ischial tuberosities. By deepening the lateral portions of this incision the ischio-rectal fossæ are exposed, and in the middle the external sphincter ani is detached from its connection with the central point of the perineum, care being taken not to cut into the bulb or the urethra at this stage. The anus and the lower portion of the rectum are now pushed backwards with the fingers and held there by a flat retractor, the knife not being used lest the gut be injured. By retracting the anus and drawing the bulb forwards there is exposed the prostate, the prostatic and membranous urethra surrounded by the constrictor urethræ muscle, the bulb covered by the bulbo-cavernosus muscle, and the transverse perineal muscles inserted into the central point. Whilst thus retracting the wound the transverse perineal and the bulbar arteries or their branches, if cut, are clamped or tied. The urethra is next opened by an exactly median incision, commencing along the median raphe of the bulbo-cavernosus muscle, and extending backwards through the membranous urethra to the prostate. It is of the greatest importance, in order to ensure rapid healing, to keep exactly in the middle line, and there is no difficulty in doing this without the aid of a staff, although a median staff, accurately held, is of assistance where the urethra is permeable. But there is no difficulty in making this median incision without any guide when the urethra and prostate have been first of

all exposed, as described. The urethral incision must be of sufficient length from the prostate forwards to allow of subsequent manipulation without any tearing.

Having opened the urethra along the middle line a probe-pointed gorget can be passed into the bladder, followed by the finger, which can now fully examine the bladder, aided by the counter-pressure of the left hand on the hypogastrium. Owing to the larger superficial wound and the free opening of the urethra, there is not required that thrusting to get the tip of the finger beyond the neck of the bladder characterising the ordinary median cystotomy, whilst lateral lithotomy opens the bladder partly by cutting, partly by tearing the left of the neck. A small speculum can be passed into the bladder and the wall viewed directly by the aid of a small electric lamp. A rectal speculum with a slit is of service in examining an enlarged middle lobe of the prostate, which will partly project into the slit. Such an enlargement can be pinched off or burnt down by the cautery in full view, whilst the speculum protects the sphincter vesicæ from injury. A firm enlargement of the prostate can be drawn downwards into fuller view by a volsella, and burnt or cut away whilst the bleeding is completely controlled. A groove can be burnt in the middle of the enlarged prostate until the level of the floor of the post-prostatic pouch is reached, which is thereby effectually drained, whilst all injury to the rectum is avoided by the preliminary retraction. Portions of an enlarged lateral lobe may be shelled out or punctured with the cautery point to promote absorption, and beyond lie the vesiculæ seminales, which are easily reached by a little further retraction of the rectum. There is ample room to use lithotomy forceps or a scoop, and to extract small or medium-sized stones from bladder pouches, or indeed to use one of the large perineal lithotrites. In cases of complicated stricture with fistulæ travelling back towards the rectum, the urethra is reached by a median incision behind the stricture, which can then be traced forwards,

and fistulous tracks outside the urethra are either excised or slit up.

After the necessary manipulations are completed the bladder can be washed out; all bleeding points are in view and may be tied, or if in the prostate touched with the cautery. It is hardly necessary to insert any plug or tube; in any case it should be removed the next day.

When the legs of the patient are brought down from the lithotomy position not only do the edges of the urethra come well into apposition along the middle line, but the transverse skin incision does so also in the folds between the anus, scrotum, and buttock. This can be clearly demonstrated by turning the patient on his side after extending the legs; the edges of the curved skin incision will be found to have come naturally into place. There is therefore no need for any sutures.

The after history of the cases will show that the leakage of urine through the perineum is surprisingly small, urine being quickly passed through the penis, whilst the flow through the perineum ceases in a week or ten days owing to the union of the urethra along the median line. Following upon this the skin wound completely unites, leaving a scar which forms a slight ridge across the perineum in front of the anus.

The classical complications, recurrent hæmorrhage and septic absorption, are absent owing to the methods of operating, the free skin incision, the deliberation of the manipulations, the exactly median incision avoiding all rupture and lateral deviation and pockets, the complete arrest of hæmorrhage, the free escape of urine afterwards.

The following cases illustrate the advantages of this operation.

A. *Urethral Stricture.*

Case 1.—A tailor, aged 49, was seen with cystitis and incontinence. His stricture had followed on several

attacks of gonorrhœa, the first twenty years before. It commenced in the penile urethra, and was completely impermeable even under an anæsthetic. The membranous urethra was opened behind the stricture, which was divided forwards to one inch in front of the posterior fold of the scrotum; anterior to this it was simply dilated. A false passage leading backwards towards the rectum was slit up completely. The patient was soundly healed two months after the operation, the urethra readily admitting a No. 16 bougie, which he was ordered to pass regularly at intervals.

Case 2.—A ropemaker, aged 37, developed a stricture following gonorrhœa twelve years before. Dilatation by bougies was attempted, but this caused great pain, with rigors, fever, and collapse, also epididymitis, and these symptoms recurred when dilatation was again attempted. Following the operation with the complete division of the stricture exactly along the middle line, a No. 16 bougie passed without any pain or other symptoms. The perineal wound soon healed and the patient was dismissed with a No. 16 bougie.

Case 3.—A draper, aged 38, suffered from a stricture which had followed several attacks of gonorrhœa, the last more than ten years before. Four years previously internal urethrotomy was done, and he learnt to pass a No. 9 to 12 metal bougie. This he could do easily at first, then with increasing difficulty, although he tried regularly, until he could no longer pass the bougie at all. Increasing frequency of micturition and straining set in until he had to pass one ounce or so every hour, night and day, after much straining. Internal urethrotomy was again attempted, and as this failed external urethrotomy by the Wheelhouse method was performed, and a perineal tube tied into the bladder to give the front part of the urethra rest. After draining for some time nothing could be satisfactorily passed. When I first saw the

man, whilst urine was escaping from the perineum, no bougie could be passed unless under an anæsthetic, when, after considerable difficulty in avoiding false passages, I passed a full-sized bougie. Still no improvement followed, nothing could be passed except under an anæsthetic on account of the false passages. I therefore operated as I have described, and after dividing the stricture throughout its whole length, exactly along the median line, I found the tracks of three very indurated sinuses leading backwards towards the rectum. Having partly excised and partly slit them up completely, I tied a catheter in the bladder through the penis, and conducted the urine off to a vessel under the bed. Continuous drainage and daily irrigation of the bladder was kept up for five weeks, when his No 12 silver catheter could be easily passed and he was dismissed, passing this catheter for himself, with the perineal wound quite healed.

With regard to alternative measures Cock's operation is valuable when there is retention with the urethra dilated behind the stricture, or when there is threatened or actual extravasation of urine, but it leaves the stricture in front and any false passages untreated. Wheelhouse's operation is sometimes very difficult, takes a long time, and unless the stricture is completely divided is apt to be unsatisfactory. Moreover false passages are left untreated, and hence there is often a difficulty, especially when the patient tries to pass his own instrument. It will be noted that the three patients were comparatively young, two under forty and one under fifty, and that the strictures were complicated. The method provided a satisfactory cure, the perineal wound healing soundly, and the patients being able to pass for themselves the largest sized bougies.

B. *Removal of Calculi.*

Case 4.—A cabdriver, aged 57, presented the following surgical history:—Six years before he had been operated

upon for stricture; three years before a stone had been crushed, but the removal was incomplete, and shortly afterwards supra-pubic lithotomy was done. It was a very difficult operation owing to the very contracted and sacculated bladder. One year before he underwent lateral lithotomy, after which there was severe recurrent hæmorrhage for a week, which had to be controlled by firmly plugging the wound. Four months before being seen by me his stricture had again been dilated and his bladder sounded without a stone being found. I thus had to deal with a patient in whom a stone had formed for the fourth time in a very contracted and sacculated bladder with a partially strictured urethra. The cicatrix of the supra-pubic lithotomy wound was very depressed, and I learnt that the operation had been difficult enough at first; to have attempted a repetition would inevitably have led to the opening of the peritoneal cavity, and its infection by alkaline urine. Lithotrity had previously failed, and lateral lithotomy had been attended by dangerous hæmorrhage.

The operation therefore was carried out as has been described; a large bulbar artery was tied on each side, the neck of the bladder reached, and a stone the size of a pullet's egg easily removed from a pouch on the left side of the trigone. Some phosphatic concretions were also scooped and washed out. At the same time the opportunity of fully dividing the imperfectly cured stricture was taken. No tube was inserted. There was no further bleeding, he began to pass urine through the penis on the third day, by the end of the week hardly any urine escaped by the perineum, and in three weeks the wound had completely healed. After the previous lateral lithotomy there had been firm plugging of the wound for a week, no urine passed through the penis for three weeks, and the perineal wound leaked for a long time.

The man continued to wash out his bladder for two years, and so remained free from any re-formation of stone. Then he began to neglect the washing out, and

gradually symptoms of stone came on again with pain in the prostate, and orchitis which went on to suppuration. I therefore repeated the operation about two and a half years later; there was not only a stone in the same pouch as before, but also a number of small calculi in the substance of the prostate, all of which were easily removed from the fully exposed organ. He likewise recovered rapidly from this repetition of the operation. Most of the urine passed through the penis within the first week, and the external wound healed in about a month; the testis also healed. When last seen the patient was in good health, and may continue so if he attends to the daily irrigation of the bladder.

Case 5.—A greengrocer, aged 40, gave the history that about a year ago burning pain had commenced in the urethra before and after micturition. Gradually the pain increased with frequent micturition and occasionally hæmaturia, so that he had to give up work. During the last two months the frequent micturition had changed to complete incontinence, with great and constant pain in the perineum and tip of the penis. When seen the patient was very pale, thin, haggard. From the urethra was escaping thick pus, as in acute gonorrhœa, but the pus was mixed with alkaline urine, for there was complete incontinence. Fæces were also being passed involuntarily, and he had superficial sores on his back and buttocks. At first sight I thought that the patient had an abscess of the prostate, but on examining *per rectum* a large stone could be felt occupying the neck of the bladder and the prostatic urethra. A sound easily struck this stone, but could not be passed beyond it. By passing the finger further into the rectum and examining bimanually with the other hand on the hypogastrium another stone could be felt above the first, but held firmly by a contracted bladder. During these manipulations thick pus spurted out from the meatus urinarius.

As the patient was in such pain and pus seemed to be

retained I operated at once by the method described. The first stone reached, oval in shape and 2 oz. in weight, was fixed in the dilated prostatic urethra and the neck of the bladder, having its long axis corresponding to that of the urethra. It was easily extracted. The second stone, also oval in shape and weighing 2¼ oz., was lying transversely with the bladder most firmly contracted over it, and articulating with the first where there is a facet, so as to form a T. This stone was manipulated bimanually so as to turn its long axis into the vertical, and was then extracted by forceps aided by a hand on the hypogastrium.

Both stones are exhibited; one has been cut and analysed; it is mainly composed of urates, and shows two nuclei fused together. After the operation the patient did not present any special symptoms; the temperature gradually became subnormal. Diarrhœa set in, and he died on the fifth day after the operation.

Post-mortem.—Both kidneys were found equally distended with non-odorous pus, the remaining cortex was riddled with small abscesses, and several abscesses existed between the cortex and the capsule. The bladder was very contracted and thickened, but not sacculated; there was a superficial ulceration of the mucous membrane with a few submucous hæmorrhages. The prostate was small and thin, but not excavated by an abscess. The pus, therefore, which flowed from the meatus mostly came, apparently, from the kidney. The operation wound was limited to the cut edges of the prostatic and membranous urethra. There was no bruising nor sloughing, nor inflammatory infiltration of any kind around the neck of the bladder.

Case 6.—A tailor, aged 41, had served in the Zulu war of 1879, where he was attacked with acute inflammation of the kidneys and continued to pass blood for three months (? endemic hæmaturia). This left a "weakness in the loins" until eight months previously, when he began to suffer from nocturnal incontinence and

passed pieces of stone. Shivering fits used to come on at night, and a week before he became rapidly worse, with great pain and frequency of micturition, straining, and incontinence. The patient looked very ill, his urine was alkaline and contained pus but not blood. On examination *per rectum* the prostate was found enlarged and very tender, and a stone was struck immediately behind it. His bladder could not be washed out owing to the pain, but it seemed very contracted. Two days before operation the patient had severe rigors, the temperature rising to 104·6° F., a pulse of 108, with abdominal tenderness and rigidity. He was in such pain that he used to sit up in bed and hold his penis. Some fragments of small calculi were passed. At the operation a normal prostate was reached, but behind it was a pouch containing many small stones, some faceted, some fractured, altogether a handful 244 grains in weight, and composed mainly of urate of ammonia. The bladder was hypertrophied and contracted. The patient lost his pain and the abdominal rigidity disappeared, but on the second day he collapsed and died.

Post mortem both pleural cavities contained fluid; the lungs were œdematous and bronchitic. There was a single horseshoe kidney which showed marked septic changes; there were several small faceted calculi in the single pelvis and passing down the two dilated ureters, and two or three had reached the bladder subsequent to the operation; at least the bladder was fully explored with the finger before terminating the operation. The bladder was intensely congested, with some hæmorrhages. The operation wound was of the strictly limited character described in the former case; it had been a very satisfactory means of reaching the pouch behind the prostate and in affording free drainage.

It is unnecessary to say much on such a well-worn topic, yet I think that these three rather exceptional cases indicate that occasionally the operation on the lines described by Celsus is definitely of advantage. The two

latter cases came under treatment too late, yet the opportunity of making a post-mortem examination showed that the operative interference was strictly limited to the middle line of the prostatic and membranous urethra. At the discussion on the removal of large stones at the Ipswich meeting of the British Medical Association much stress was laid upon perineal lithotrity for large calculi. The wound I have made would readily admit the large lithotrites shown at that meeting.

c. *Prostatic Obstruction.*

Case 7.—A healthy-looking man aged 72, employed as a messenger, had had increasing pain and frequency of micturition for two years, until finally he passed 1 to 2 oz. of urine every hour, day and night. A sound entered a contracted bladder and so pushed back a middle lobe of the prostate that it could be felt *per rectum*. All instrumentation caused much pain, and the bladder would not allow of more than 1½ oz. of water being injected. A fortnight of treatment in bed with drugs in no way improved the patient, and micturition occurred every half-hour to one hour, day and night. The prostate was easily reached at the operation, and a soft pedunculated middle lobe was found, with a collar surrounding the orifice of the contracted bladder. Pieces were plucked away by punch forceps and the rest burnt down with the cautery, guarded by a rectal speculum with a longitudinal slit. A phosphatic concretion the size of a field pea was removed. The patient passed 3 oz. of fluid through the penis on the third day. As he was quite relieved he slept well and rapidly recovered. Fourteen days after the operation the perineal wound had quite healed. He returned to his work as a messenger, and when seen subsequently had no further trouble.

Cases 8 and 9.—I have had two other successful cases in patients about sixty, the obstruction being mainly a

collar-like projection with a small bladder. They returned to work without need of further instrumental or other treatment.

A fourth case was unsuccessful.

Case 10.—An Italian wire-worker, aged 58, had had difficult micturition for two years, and had lately very much pain, passing a few drops of urine only at a time. He had an earthy, wasted look, and was very weak. The urine was of low specific gravity, and contained some albumen. No catheter could be passed except a silver one, and that with difficulty. On reaching the prostate two very vascular lateral lobes were found joined by a high ridge which projected into the bladder, having behind it a deep bladder pouch. Through the slit of a rectal speculum the ridge was burnt away until a deep channel was made between the lateral lobes, affording a complete drain for the pouch. The patient at first improved, and a fortnight after the operation got up. He passed water through the penis; the bladder was emptied, and the urine lost its albumen. However, his pulse never sank below 100, nocturnal delirium and then a typhoid condition supervened, and he died a month after the operation. The perineal wound, although healthy, had not completely healed. Unfortunately a post-mortem examination was not allowed, but he apparently died from chronic nephritis.

Prostatectomy has the advantage of being a radical method when the patient is relatively young and strong enough. If successful the patient may return to his occupation, and especially among the poor there are great difficulties in carrying out treatment depending upon catheterism or involving continuous medical attendance, and many patients therefore become paupers.

Supra-pubic prostatectomy is best done when there is a large bladder and a pedunculated middle lobe. A contracted bladder and a post-prostatic pouch with enlargement of the lateral lobes are not so favourable conditions. I have

operated by the supra-pubic method when the bladder was contracted with the prostatic obstruction mainly like a collar, and although the patient did well, yet the operation was difficult, no good view could be obtained, and therefore recurrent hæmorrhage might well have taken place. As regards other ways of performing perineal prostatectomy, there is not such good exposure of the prostate, and the cauterisation by Bottini's and other methods is done in the dark, which, if the cautery is too hot, may lead to hæmorrhage and sloughing. If performed as described there is no danger of a perineal fistula, although this would be a trivial matter as compared with a supra-pubic one. Castration and vasectomy appear to be very uncertain in their results, and leave a post-prostatic pouch undrained, with possibly a calculus in it, so that renal complications progress.

Conclusion.—The cases quoted indicate that this operation is especially applicable to certain instances of complicated stricture, bladder calculi, and prostatic obstruction. The unsuccessful cases have shown too advanced disease of the kidneys. When this complication had not set in the results were good.

DISCUSSION.

Mr. Clement Lucas.—The author recommends the procedure for three classes of cases—old strictures with false passages, exceptional cases of stone, and in certain cases of prostatic obstruction. The cases of stricture, it seems to me, are those in which this operation is least valuable, because there are other methods of treating such conditions successfully. I think he scarcely did justice to Cock's operation when he suggested that it is valuable, more particularly in cases of retention of urine. It is certainly valuable in many conditions not associated with retention, conditions in which the perineum and scrotum are riddled with sinuses, for instance, in which the inflammatory swelling subsides, when the urinary stream is diverted, and soon after the stricture becomes permeable. I should imagine, therefore, that the cases in which this operation (which allows one to reach the bladder with ease and directness) is desirable are not particularly those of stricture, but cases of prostatic hypertrophy, where part of the prostate may require to be removed. To be able thoroughly to expose the bladder,—to expose its interior from below, is, I hold, an important thing. It may also prove useful in certain cases of lithotomy. I have no experience whatever of the operation, but in the cases which I have indicated, I shall certainly at some future time utilise the author's suggestion.

Mr. Freyer.—I think this operation may be valuable for an enlargement of one or both of the lateral lobes of the prostate, but the middle lobe could better be removed by the suprapubic method. Mr. Spencer thinks it unnecessary to drain by means of a tube. Personally, I should be afraid to allow the urine to pass over such a large surface, and I should feel more inclined to tie in a perineal tube, and drain the urine away from the bladder clear of the wound for at least five or six days, so as to give the superficial perineal incision an opportunity of uniting before the urine came into contact with it. In regard to stricture I consider that Wheelhouse's operation is preferable. I operate by his method with instruments modified by Guyon, of Paris, and by myself. As to Cock's operation I was under the impression that it had been obliterated from surgery. I myself do not remember to have seen one case during the four years I have been attached to St. Peter's Hospital or in private practice. I myself have not done it for at least twelve years. One aspirates the bladder supra-pubically now as a temporary measure, and then has recourse to Wheelhouse's operation. I regret that in face of the discussion that has just taken place,

in spite of several papers in the medical journals, and particularly after the discussion at Ipswich, Mr. Spencer should talk about "lateral lithotomy, which has rightly lapsed into disuse." Does he mean to say in face of statistics that lateral lithotomy has rightly lapsed into disuse in comparison with the supra-pubic operation? I myself practise litholapaxy extensively, and rarely have recourse to lithotomy of any kind. If, however, we compare the perineal method with the supra-pubic operation I am surprised that he should make use of such words. It has not lapsed into disuse. It is extensively employed, and very successfully so, in India at the present time, and also in one of the children's hospitals in London. Gilbert Barling states that in one of the children's hospitals between 1888 and 1893 inclusive, twenty-two cases were operated on, fifteen by the lateral and eight by the high operation, and that all the lateral operations were recovered from, while four of the others died.

Mr. CHRISTOPHER HEATH.—This subject comes up periodically. In 1860 the late Mr. John Wood read a paper in this Society embodying a good deal of what the author has brought forward to-night, even to having a curved incision, though apparently his curved incision did not go right across the perineum. I think myself that it is not a matter of very great importance what way it is made, provided it is sufficiently free. I agree with what the author says as to the necessity of having plenty of room, and that is the drawback of Cock's operation. I know that it has been fairly successful, and that it is still done at Guy's, though that is, I believe, the only institution where it is done. In practice it was found more difficult to hit off the membranous urethra from the perineum than Cock and his pupils had apparently found it. After all we are not much advanced upon the old method of median lithotomy. What used to be called Allarton's operation was opening the membranous urethra and dilating the prostate, but no one would hesitate, if necessary, to make a cut on each side. In spite of what Mr. Freyer has said, I think lateral lithotomy has fallen into disuse, and the students of the present time very seldom see it performed. I think the author has done service by reviving the perineal operation in a modified form. I remember being sent for to a case of retention of urine, and I made a median incision and removed a large stone, and everything did admirably. In cases of that kind, where the perineal operation is to be preferred, whether by median or semicircular incision is not of much importance, so long as you do not wound the roof of the membranous urethra. One must therefore be very careful only to open the floor, and then to pass some blunt instrument in order to get a good guide into the bladder through the prostate. Cases of prostatectomy are rather rare

nowadays, but I quite think that in such cases as the author has mentioned he did the best for his patient.

Mr. W. G. SPENCER.—Cock's operation, as far as I know it, seems to be most frequently done in cases of large extravasations of urine met with in hospital. It is rather difficult to hit off the undilated membranous urethra, though with special skill no doubt the operation is a valuable one. With regard to the draining operation for the cure of sinuses it had proved useless in Case 3. After the proposed operation there is really no obstacle to the outflow of urine, which must come away through the perineum. Why, then, use a tube, which is a sure source of irritation? With regard to Wheelhouse's operation, I remarked that in one of my cases it had been already done, and I am sure the surgeon had done it well, but it had not proved successful, and I submit that it is sometimes a difficult operation. Unless you can get into the line of the urethra and follow it back your patient is not likely to do well, and you will often leave sinuses. The great thing is to get into the healthy urethra behind the stricture and follow it forwards. Mine is a deliberate operation, whereas Cock's is a happy shot through the perineum. In all post-mortem examinations of cases of lateral lithotomy I maintain that it has been proved that great harm happens in clumsy hands from injury to the urethra. I submit that the success of lateral lithotomy was by so much as it was not lateral but really median as regards the urethra. The objection to the median operation has been that there is so little room, but in the operation described in the paper the ample superficial incision allows one to get the full benefit from median urethrotomy. I must still hold that lateral lithotomy, involving the tearing into the loose connective tissue around the neck of the bladder, is a bad operation, and should be dismissed. I have not included Mr. Wood's [1] paper because it really deals with Civiale's method, using special instruments for forcibly distending the urethra and prostate by stretching it. The important thing is to have a free incision, the shape being not of much importance. The advantage of the semilunar incision is that it falls into the natural folds of the scrotum and buttock, as you can see when the patient is turned on his side. It thus heals with great readiness without the necessity of putting in sutures which might retain urine behind them.

[1] Wood, J., "On an Operation for extracting a Stone from the Bladder by Urethrotomy, and Dilatation of the Prostatic Urethra by means of an Expanding Staff; with Remarks on the Relative Anatomy of the Perineum and Pelvic Viscera" (Abstract), 'Proceedings of the Roy. Med. and Chir. Soc.,' 1861, vol. iii, p. 310.

ARTERIAL HÆMORRHAGE FROM THE EAR

AND ITS

CONTROL BY LIGATURE OF THE COMMON CAROTID ARTERY

BY

WALTER G. SPENCER

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ARTERIAL hæmorrhage from the ear, Otorrhagia, recurring so as to threaten or cause death, is a rare complication of middle ear disease. Toynbee, in vol. xliii, p. 217, of the Society's 'Transactions,' described a case under the heading "Acute Caries of the Walls of the Tympanic Cavity producing Ulceration of the Internal Carotid." The subject is also considered in the larger textbooks, *e. g.* Schwartze's 'Deutsche Chirurgie,' Lief. xxxii, 1885, S. 406; 'Politzer,' translated by Dalby and Dodd, 1894, p. 482.

In some twenty recorded cases, death from hæmorrhage has been shown by post-mortem examination to have been caused by ulceration into the internal carotid artery in the carotid canal. These post-mortem examinations give a very unfavourable aspect to the cases, for

in all the disease has been far advanced. But where the inflammation has been of quite recent origin, ligature of the carotid has been followed by cessation of the hæmor-

FIG. 1.

The Carotico-tympanic Septum.—Upper half of a horizontal section through the right pars petrosa (Rüdinger, 'Atlas der menschlichen Gehörorganes,' 1875, Lief. ii, Taf. i, Fig. 2).

Between 22, the tympanum, and 24, the carotid canal, is the septum, which is perforated by the carotico-tympanic canal.

(20. Meatus auditorius externus; 21. Sulcus tympanicus; 23. Stapes at its insertion in the fenestra ovalis; 25. Vestibule; 26. Cochlea, first turn; 27. Meatus auditorius internus.)

rhage. This success was first obtained by Syme in a classical case, and more recently by Brown and Stewart, as well as in the case to be described by me. I propose

in this paper to divide the cases which have occurred into three groups, the first two unfavourable, the third group, if treated early, favourable for the operation. In all the cases to be mentioned below, the hæmorrhage showed itself quite uncontrollable except by compression or ligature of the carotid, ceasing for a time when the patient fainted, but tending to recur at short intervals until death. The blood forced itself out of the ear in spite of plugging, or passed down the Eustachian tube and out by the nose and mouth; or the blood was swallowed and then vomited, or passed as melæna.

I. *Cases entirely Unfavourable on account of being Secondary to Pulmonary Tuberculosis.*

Some of the cases examined post-mortem would have been in any case fatal, for they had been attacked by rapidly progressive tuberculous caries and necrosis secondary to pulmonary tuberculosis. The septum between the anterior part of the tympanum and the carotid canal (see Fig. 1) was found perforated or destroyed with the formation of sequestra, putting the artery in free communication with the cavity which had replaced the middle ear. The artery itself was separated from its canal and surrounded by pus, its wall thickened and softened, presenting erosions from the jagged sequestra, and one or more perforations at or close to the angle made by the artery in changing from its vertical to its horizontal course. Thus death occurred exceptionally by one sudden and furious hæmorrhage; generally the hæmorrhage ceased with the fainting of the patient, and recurred several times within a few hours, or a day or two before occasioning death. No clot was found in the artery, except in the ligatured cases.

Toynbee's case ('Med.-Chir. Trans.,' 1860, vol. xliii, p. 217).—A man aged 46 had had for a long time progressive pulmonary tuberculosis, and for four years a stinking

left otorrhœa. His cough started the hæmorrhage, for which, after the second bleeding, ligature of the carotid was proposed and declined. The hæmorrhage recurred every eight or ten hours for thirteen days. When the patient died an ulcerated opening into the artery two lines in diameter was found. The disease of the petrous bone had not extended to the lateral sinus or cranial cavity.

Chassaignac's case ('Traité de la Suppuration,' t. i, p. 529).—A man aged 50 had pulmonary tuberculosis of long standing, and for six months right ear disease, with deafness and facial paralysis. The pus was for a time bloodstained; then severe hæmorrhage took place three times at intervals of a day and two days. After death, following upon the last hæmorrhage, the lumen of the carotid was found to communicate by a wide opening with the carious cavity replacing the middle ear. A large clot had become extravasated beneath the dura mater, partly in the anterior, partly in the middle cerebral fossa.

Marcé's case ('Bull. de la Soc. Anat. de Paris,' 1873, année xlviii, p. 829).—A patient with advanced phthisis had had otorrhœa on the right side for a year and had become deaf, when suddenly, whilst in bed and asleep, towards early morning, hæmorrhage from the ear occurred, ceased after a few minutes, recurred some few hours later, when 250 to 300 c.c. were lost, and was followed by further attacks at short intervals, until the sixth proved fatal. The internal carotid was found to communicate with a carious cavity in the position of the middle ear, which was full of blood and pus.

Politzer's case ('Text-book of the Diseases of the Ear,' English translation from 3rd edit. by Dalby and Dodd, 1894, p. 483).—A phthisical individual aged 32, who had died of hæmorrhage, showed a sharply-cut oval opening from the tympanum into the carotid canal, with an even larger perforation into the eroded artery.

Hessler's case ('Archiv f. Ohrenheilkunde,' 1882, Bd. xviii, S. 1).—A woman aged 42 had been in hospital three months with progressive pulmonary tuberculosis of nine months' duration, and a purulent discharge from both ears, which had existed six months. Suddenly, whilst sitting up in bed, an enormous hæmorrhage occurred, spurting out from the right ear in a bright red stream and pouring into the throat. Death took place in four or five minutes. The carious right ear freely communicated with the carotid canal; the septum had formed sequestra, and on the anterior and inner side of the angle of the carotid artery was an opening 4 mm. long and 2 mm. broad, with ragged edges, and a discoloration of the wall of the artery for 2 cm.

In two cases similar to the above the carotid was tied.

Baizeau's case ('Bull. de la Soc. de Chirurgie,' 1861, 2e sér., t. ii, p. 430).—A soldier aged 23 had a number of tuberculous lesions in the lungs, knee, elbow, omentum, and cheek. Otitis media purulenta with complete deafness had existed in the left ear for ten months, when after coughing a small hæmorrhage occurred, followed by a second four days later, and a third eight days after the first. A hæmorrhage of a minute's duration occurred on the ninth and tenth day. On the seventeenth day the left common carotid was tied, but after twenty-four hours there were again repeated hæmorrhages, and death took place three day after the operation. Two jagged sequestra, one the size of a rice grain, the other of a large pea, formed from the septum between the tympanum and the carotid canal, had ulcerated into the internal carotid at its curve, causing two openings close to each other about $\frac{2}{3}$ mm. in diameter. Septic softening had set in in the left parietal lobe of the brain.

Broca's case ('Bull. de la Soc. de Chirurgie,' 1866, 2e sér., t. vii, p. 172).—A man aged 47 had had a cough for a year, and for two months purulent discharge and deafness

from the right ear. Suddenly, whilst at work, there was severe hæmorrhage, and this recurred every three or four days, generally from the ear; only once did the blood pass into the throat. After six weeks from the first hæmorrhage the right common carotid was tied 1·5 cm. below the bifurcation. A little oozing of blood continued from the ear; the ligature came away without hæmorrhage from the neck twenty days after. Death took place from rapidly progressive tuberculosis a month later. A clot was found in the internal carotid extending from the distal side of the ligature into the carotid canal. The hæmorrhage had taken place through an ulceration in the wall of the artery at this point into the carious middle ear.

II. *Cases of Chronic Ear Disease.*

Cases such as the following are now subjected to surgical treatment, and I have not met with any recent case in which arterial hæmorrhage has occurred.

Choyau's case ('Bull. de la Soc. Anat.,' 1864, année xxxix, p. 384).—Three hæmorrhages took place from the nose and ear before death; the second was measured and amounted to 1½ litre. A wide communication between the tympanum and carotid canal was found with two holes into the carotid close to its curve, whilst the artery in the canal was softened and thickened.

Grossmann's case ('Schmidt's Jahrbuch,' 1870, Bd. cxlviii, S. 250).—Bleeding recurred several times, and the patient died nine days after the first hæmorrhage. There was a perforation into the carotid at its angle more than 3 mm. in circumference.

Hermann's case ('Wiener med. Wochenschrift,' 1867, pp. 471, 486, 503).—Bleeding began suddenly from the left ear, and recurred every day for a week. After death

there was found a free communication between the tympanum and the carotid canal four lines in length, and an opening into the artery two lines long and one and a half broad.

Sokolowski's case ('Centralblatt f. Chirurgie,' 1881, S. 62).—Blood to the amount of 1 to 1¼ kilogram suddenly flowed from the ear, and hæmorrhage recurred daily from the ear and mouth until death, twelve days after the first hæmorrhage. A large cavity filled with tarry fluid had been formed by destruction of the middle ear, into which the carotid projected, having on its outer and lower wall a hole ¾ cm. in length.

Boinet's case ('Archives gén. de Méd.,' 1837, 3e sér., t. ii, p. 339, obs. x).—A very advanced case of ear disease. Hæmorrhage from the nose, mouth, and left ear started quite suddenly whilst the patient was talking, and ceased in about two minutes, leaving the patient pulseless. A second hæmorrhage happened the next morning, and the third, fatal one, the following evening. There was most extensive destruction of the petrous bone, including the facial nerve, but the dura mater and cranial contents were normal. On the wall of the internal carotid in the middle of its course through the carotid canal was a perforating ulcer about one line in diameter.

It may be that the hæmorrhage was favoured by excessive doses of mercury in some of the cases recorded.

Billroth's case ('Archiv f. Ohrenheilkunde,' 1869, iv, S. 53).—A man aged 27 was undergoing a course of mercurial inunction when he was seized with severe pain in the right ear followed by the outflow of eight ounces of blood, which recurred generally every day for a fortnight, the blood being mixed with muco-pus, which escaped both externally and by the Eustachian tube. The right

carotid was thereupon ligatured and the bleeding stopped for nine days. Then it began again more severely from the ear, nose, and throat, and, fourteen days after the right, the left carotid was tied. Three days later the most copious hæmorrhage of all occurred, from which the man died. An opening was found in the internal carotid just before its bend in the carotid canal, 8 mm. long and 6 mm. broad, from which the blood had escaped into the external auditory meatus without the membrana tympani having been perforated.

Ward's case (Pathological Society's 'Transactions,' 1846, vol. i, p. 38).—This case, although the ulceration took place into the middle meningeal and not into the internal carotid, suggests also the evil influence of excessive treatment by mercury. A girl of sixteen was treated by a course of mercury to salivation, which much increased a foul discharge from the ear, and the soft parts became necrotic. Six weeks after the commencement of the treatment two severe hæmorrhages occurred from the ear, followed by death, without any paralysis or loss of consciousness having been noticed. Necrosis extending from the petrous bone had involved the temporo-maxillary joint and the dura mater of the middle cerebral fossa, where a branch of the middle meningeal had been perforated. Blood and pus had been extravasated over the left hemisphere of the brain.

III. *Hæmorrhage in Cases of Recent Inflammation.*

In a third group of cases the hæmorrhage has arisen in cases of quite recent inflammation, more or less acute. I have not met with any submitted to post-mortem examination, so that the exact arterial lesion remains undetermined.

Porter's case (Graves's 'Clinical Lectures on the Practice of Medicine,' 1848, vol. i, p. 342).—A boy aged eleven

after scarlet fever had suppuration in the glands of the neck and bilateral otorrhœa. On the right side the discharge became foul and facial paralysis set in. Suddenly, in the ninth week, severe arterial bleeding from the right ear, mouth, and nose supervened, ceasing when the patient became faint. It recurred several times, and the patient died in the thirteenth week. There was no post-mortem examination.

Hyne's case ('Lancet,' 1870, vol. ii, p. 431).—A boy aged 4 had an attack of scarlet fever complicated by acute nephritis, and on the fourteenth day by a purulent discharge from the right ear. He was progressing well, sitting up in bed, with a good appetite, when suddenly on the twenty-fifth day there was severe hæmorrhage by jets from the right ear. A few hours later much blood was vomited, and melæna passed. The hæmorrhage from the ear and mouth recurred on the next day, and soon led to death. No post-mortem examination is mentioned.

Cases successfully controlled by Ligature of the Carotid.

Syme's case ('Edin. Med. and Surg. Journ.,' 1833, vol. xxxix, p. 319).—A boy aged 9 had an acute swelling of the right fauces, followed by a painful swelling in the neck between the larynx and right sterno-mastoid muscle. This gradually enlarged upwards to the jaw and to the ear, and on the tenth day a cupful of pure pus was discharged through the external auditory meatus. The next evening bleeding to the extent of some ounces occurred from the ear; it ceased spontaneously, but recurred later several times both from the ear and mouth, whilst the swelling in the neck increased without any distinct pulsation. Therefore eighteen days after the onset Syme tied the right common carotid. Hæmorrhage again recurred several times, but definitely stopped three weeks

after the operation. The swelling in the neck subsided, and three months later the child appeared well.

Brown's case ('Lancet,' 1898, vol. i, p. 1536).—A girl aged 5 had an attack of follicular tonsillitis, which was apparently clearing up when, without warning, hæmorrhage took place from the right ear, the amount lost being very great. Four days later there had been a little discharge of non-odorous pus, when a second hæmorrhage occurred more severe than the first, rendering the patient extremely anæmic and almost pulseless. In the pharynx a swelling which did not pulsate had pushed the right tonsil over towards the middle line. The right common carotid was ligatured at the level of the cricoid cartilage. The child made a somewhat tardy yet complete recovery.

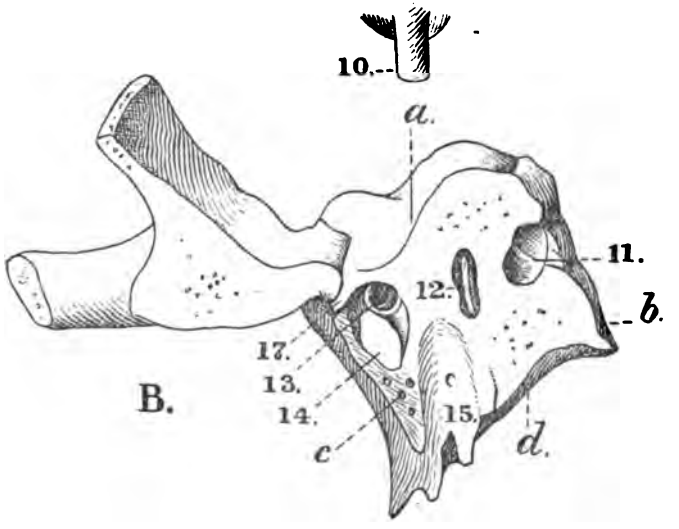
Stewart's case ('Lancet,' 1899, vol. i, p. 451).—A girl aged 3 got thoroughly wet, and a few days later developed a lump at the left angle of the jaw with pain on swallowing. Fourteen days after this intense earache was followed by a profuse discharge of foul greenish pus from the left meatus, and forty-eight hours later by the first attack of hæmorrhage. A second hæmorrhage occurred on the same day, and two more on the day following; each time the hæmorrhage terminated with faintness. The meatus was packed, and pressure applied by means of a bandage, but the bleeding recurred, and so the left common carotid was tied. This was followed by a good recovery. The colour of the blood lost was venous.

Author's Case.

A previously healthy boy aged 4 was admitted to the Westminster Hospital for hæmorrhage from the left ear and throat on December 17th, 1900. He had had scarlet fever, and was in a fever hospital from August 9th to November 7th. On the day before admission he had had a severe hæmorrhage from the ear, nose, and mouth.

When admitted, bright arterial blood was dropping from his left ear and flowing from his nose, also some clot was vomited. Mr. Payne, the house surgeon, firmly plugged the nose and ear, and fixed a pledget in the upper naso-pharynx. Twelve hours later he was seen by me for

FIG. 2.



The Carotico-tympanic Canal.—Transverse section of the petrous bone through the external third of the lower opening of the carotid canal (Testut, 'Traité d'Anatomie humaine,' 4me éd., 1899, tom. i, Fig. 141 B, p. 152).

15. Carotid canal. On the external wall of the ascending portion of the carotid canal is a small circular orifice, the lower opening of the carotico-tympanic canal.

c. The carotico-tympanic canal in oblique section. It gives passage to an arteriole, a branch of the internal carotid, and to a small nerve-filament which connects the nerve of Jacobson with the carotid plexus.

(11. Internal auditory meatus; 12. Cochlea; 13. Canal of tensor tympani; 14. Bony wall of Eustachian tube; 17. Tegmen tympani.)

recurrent hæmorrhage, and I repeated the plugging. Five hours later the fourth hæmorrhage took place, rendering him unconscious, almost pulseless at the wrist, much blood having flowed from the ear, nose, and mouth;

also some had been vomited or passed *per anum*. The left common carotid was ligatured low down in the neck by tying a kangaroo-tail tendon tightly. Meanwhile saline fluid, more than two pints, was infused into the cellular tissue of each axilla and flank, causing swellings the size of his head. At the end of the operation the pulse had improved, no more hæmorrhage occurred, all the saline fluid was quickly absorbed. The patient would not let his ear be looked at until January 9th, when a small healing perforation was seen in the upper and anterior quadrant of the membrana tympani. After this the boy completely recovered.

Conclusions.—From the foregoing account it is clear that the third group of cases, viz. those where the hæmorrhage has followed on an acute inflammation, are the most favourable for the operation. The reported cases have all occurred in children. The most likely source of the bleeding, in the absence of demonstrable evidence, appears to be the twig given off by the internal carotid to the tympanum,—ramulus carotico-tympanicus (see Fig. 2). An ulceration into this small vessel close to its origin would account for the free hæmorrhage, and yet a clot would be likely to form should the carotid be tied, for in spite of the retrograde flow from the circle of Willis, the effect of the ligature must be to reduce the blood-pressure in the internal carotid to not more than one third of its previous amount. It is difficult to suppose that the wall of the artery itself could have been perforated and yet no retrograde hæmorrhage have followed the ligature of the common carotid. The other possible sources of the hæmorrhage are tympanic branches from the internal maxillary or middle meningeal, or ulceration into some of the branches of these arteries outside the base of the skull; but a consideration of the severity of the hæmorrhage in the cases under consideration certainly favours an origin close to the main trunk.

The first and second group of cases were all essentially unfavourable on account of the advanced state of the

disease. The first group were especially so, because secondary to progressive pulmonary tuberculosis. Yet Broca's case in particular suggests that the operation of ligature of the carotid is advisable as a palliative measure.

As to the second group, those of neglected chronic ear disease, the extension of the disease would now be prevented, or should be so. In the advanced cases examined post mortem, the perforations have been all at the same point of the artery, close to its angle. It would seem likely that the perforation has been reached by ulceration travelling back along the carotico-tympanic twig to the wall of the artery itself. Hence it may always be possible, even where hæmorrhage supervenes in old-standing disease, that the ulceration may be still confined to the origin of the above branch. When, however, there is a wide opening into the carotid itself, retrograde hæmorrhage is inevitable, and, as seen in Billroth's case, nothing more is to be gained by ligaturing the artery of the opposite side. So free is the anastomosis that no further reduction in the blood-pressure is gained thereby.

It is certainly the common carotid which should be selected for ligature, not the internal. The operation is easier and quicker, and the operation wound is further away from the septic focus in and around the ear. Besides, it is not certain but that hæmorrhage may come, as in Ward's case, from one of the branches of the external carotid, the internal maxillary, or middle meningeal.

DISCUSSION.

Mr. McAdam Eccles.—These cases are extremely rare, but they are nevertheless very interesting and important. Moreover they are anxious ones, as must be all cases of ulceration into vessels. The author does not state whether any active treatment of the ear was adopted after the ligature of the carotid. I should like to know whether he considers it right or needful to undertake any active treatment of the ear condition which has set up the hæmorrhage immediately after the ligature of the artery. Then, again, does he advise ligature in every one of these cases rather than attempting initial plugging? Further, has the author had any experience in other cases of ligature of the common carotid, in young subjects particularly, in which cerebral trouble has resulted? Ten days ago I had to tie the common carotid for secondary hæmorrhage from a branch probably of the external carotid in a child of 2, who was almost pulseless from the hæmorrhage. Since that time she has had no further bleeding, and the wound—which was a sloughing one in the neck—has steadily progressed towards healing, and she has shown no sign so far of any cerebral trouble. With regard to the source of the hæmorrhage his explanation is probably the correct one in the cases in which there is not furious and suddenly fatal hæmorrhage, *i. e.* a small branch has been ulcerated into close to where it arises from the intra-osseous portion of the internal carotid.

Mr. W. G. Spencer.—With respect to the treatment of the ear condition, this child was very restless, and we did nothing in order to keep the neck quiet. It was some time before he would let the nurse even syringe out the ear, but in the course of five weeks, when I examined the ear, the otitis media seemed to have cleared up, and so he was left alone. It must be a very difficult question to decide whether or not to treat the ear after ligature, because it is quite possible, in extensive caries, to enter the carotid canal. I suppose Mr. Eccles will agree with me that even in extensive ear disease surgeons avoid the carotid canal, but where it has been perforated it may conceivably be easy to set up hæmorrhage. I do not know of a case where this accident has happened during an operation. I think, on the whole, that after ligature it is better to employ only simple means, unless there is some urgent indication for interference, such as extension of suppuration. Plugging had been tried in most of the cases mentioned, but it was of no use at all. There are, of course, slight cases of hæmorrhage which yield to plugging, a measure which everyone would of course try to begin

with. I have looked through the cases of ligature of the common carotid in children, and I do not find that cerebral trouble followed. As he is doubtless aware, cases of cerebral softening are much more infrequent now than formerly, although some have been recently recorded, but in those the surgeon was unfortunate enough to start on a septic case, or he had been operating on a patient whose arteries were already diseased. I have heard of a good number of cases of dangerous hæmorrhage in the neck after tuberculous glands, possibly because surgeons deal with them more freely now than they used to, or because they are more venturesome. I can recall one or two cases of death even after such hæmorrhage, owing to its coming on at night, so that some caution in these operations is desirable. In other cases of sudden death from hæmorrhage from the ear or throat there has been no post-mortem, but no doubt, in ulceration of the carotid, death is sometimes quite sudden, as in one of the cases referred to in the paper.

A CONTRIBUTION

TO THE

STUDY OF INTESTINAL SAND

WITH NOTES ON A CASE IN WHICH IT WAS PASSED

BY

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THE occurrence of intestinal sand has attracted the attention of observers for some years past. Cases presenting this symptom appear to have been of singular infrequency in the British Isles, for it is scarcely possible that they can have been often overlooked. English literature on the subject is, however, almost a blank, and the best text-books in this country and in the United States of America make but little reference to it. A good many cases have been noted and reported on the continent of Europe. The object of this communication is to attempt

to place these examples of intestinal sand in their proper nosological position, and to record a case of true, as distinguished from false, enteric lithiasis which came under our observation in this country. The particulars of it are as follows:

A married lady, aged 33, residing in the provinces, and leading a healthy life, began to suffer from diarrhœa early in 1900, and came under the care of Dr. Surridge. No cause for this ailment was made out. The previous health had always been fairly good. The last confinement occurred three years ago. The house occupied by this lady is built on a sandy soil, and its drainage is reported to be in excellent condition and of recent arrangement. The water-supply is not good, being hard, and containing some organic impurities.

The family history was as follows:—Both parents are living. The father is a gouty man, and a brother and sister of his are gouty. There are five sisters and two brothers; one of the latter suffers from colic. Bowel disorders are said to be prevalent in the family. The youngest sister of the patient, twenty years her junior, suffered badly at one time from a wide-spread eczema. When this disorder was subdued she suffered from asthma, the two conditions alternating. After local treatment and internal medication with arsenic, she recovered her health. The patient has two daughters aged respectively seven and three years, both in good health.

After the last confinement this lady suffered occasionally from eczema around the anus for about eighteen months. When this condition yielded to local and general treatment she became subject to looseness of the bowels, having previously been of a constipated habit. Her weight in the summer of 1899 was nine stones and two pounds.

The present ailment began in January, 1900, with a very intractable diarrhœa, accompanied with internal rumbling and purring noises, there being six or eight loose motions in each twenty-four hours.

In the middle of February the patient took to her bed, and was ordered an exclusively milk diet with lime-water. This treatment lessened the diarrhœa to three or four motions each day, sometimes attended with the passage of mucus. On the 8th of March she was seen in consultation with Dr. Harris, of Manchester. Ten days later sand was discovered in the motions, and found subsequently in all in which it was looked for.

On the 23rd March, in Dr. Harris's absence, Dr. Dreschfeld's opinion was taken on the case. No ordinary methods of treatment had any effect in checking the diarrhœa and the formation of intestinal sand. The patient was sent up to London in April, and, in my absence from town, came under the care of Dr. Garrod. At this time two or three motions were passed each day. They were loose, brown in colour, and on tilting the bed-pan the gritty sand could be seen at the bottom of the vessel, each motion containing about a teaspoonful of it. Early in May I saw the patient with Dr. Garrod. She was pallid and sparely nourished. The thoracic organs were healthy. On examining the abdomen it was found that the colon and its sigmoid flexure were, though empty, too readily palpable, and apparently thickened in their walls. The right kidney was movable. There was a slight degree of pyrexia at this period, the temperature rising occasionally to 100° or a little above this. Specimens of the sand were obtained and submitted to examination. Full details of this are furnished in Dr. Garrod's report herewith. It will suffice to say here that it much resembled at first sight a deposit of uric acid, being of reddish-brown colour and finely gritty. It was insoluble in cold and boiling liquor potassæ, and readily soluble in boiling nitric acid. Under a low power of the microscope particles of various shapes and sizes were seen, of a brilliant reddish-brown hue, and translucent.

The patient was confined to bed and kept on milk diet. For medicine, salicylate of bismuth and bicarbonate of sodium were given in mixture. Under this treatment the

diarrhœa was somewhat checked and the general health improved. The motions were rather more consistent, stained by the bismuth, but still contained sand. Towards the end of May the patient sat up for some time daily and went out for short walks, but there was now complaint for the first time of pain in the large bowel. Chicken broth, turtle soup, mutton broth, and koumiss were now given, and a mixture containing carbonate of bismuth, opium, and tincture of cinnamon. There was gradual improvement in most respects, less pain, but a good deal of rumbling noise in the bowels. The patient returned home early in June and continued the treatment under Dr. Surridge's care. Some benefit was gained by taking Bael jelly, and also from a mixture containing some aromatic sulphuric acid, tincture of cinnamon, and opium. In July, by our advice, she went to Plombières under the care of Dr. Bottentuit. She took baths and had rectal douches, and drank the water in small quantities. All vegetable food was withheld, and digestion was found to be much more comfortable without it, as it caused immediate distension. She lost ten pounds in weight while at Plombières. The next month was spent in Folkestone with some benefit, and some weight was regained.

On her return home she reported herself very much better. Her general health and her nervous tone had improved. There was still diarrhœa, with much flatulence at intervals, and some, though less, sand, accompanied with a great deal of mucus. Dr. Bottentuit prescribed bicarbonate of sodium in teaspoonful doses with advantage for the flatulent attacks. The appetite was better, and more variety of food could be borne. During October there were alternations of constipation and diarrhœa, and a considerable quantity of sand was passed on October 12th. She was next seen in November. She was rather pallid and languid, was easily tired on exertion, but had regained her usual weight, nine stones and two pounds. The large bowel no longer appeared thickened, as it did

six months previously, but there was tenderness on pressure about the splenic flexure of it. There was still a looseness of the bowel, two to four actions occurring daily, but no sand was passed. Her diet was altogether of animal food, and a little whisky was taken with one meal. The urine was turbid with lithates and deposited uric acid. The tongue was large, flabby, and thinly grooved. A mixture with liquid extracts of cinchona and bael and tincture of cinnamon was ordered, and milk with natural seltzer water was added to her diet. The catamenia were regular. She returned home about the middle of the month.

This case presented most of the characters that have been described in the few instances of the disorder that are already on record. It was, however, remarkable for the little pain which was experienced. In most examples of enteric lithiasis this appears to be a marked feature, occurring in paroxysms, lasting several hours, somewhat akin to those associated with biliary and renal colic, and attended with much flatulent distension and vomiting. According to M. Dieulafoy, who has recorded a series of these cases, there is commonly a family history of gout, and he regards the condition as one of the irregular manifestations of this disorder in many, but not in all, instances. In this case there was a distinct gouty history on the father's side. In a large proportion of the recorded cases there has been noted the co-existence of muco-colitis, often attended with the passage of mucous casts and shreds. Diarrhœa occurs in some cases, and constipation in others. The subjects of the disorder in two thirds of the cases have been women, and the average age is about thirty-five years. Examples of it have been recorded in children under four years of age. Some of the cases described by Continental observers, as will appear from Dr. Garrod's inquiries, are not truly cases of enteric lithiasis, such as that here described, the so-called sand having been proved to consist of vegetable *débris* and not of inorganic matter.

Characters and Composition of the Intestinal Sand.

When washed and dried in the air, the gritty material passed with the motions had the appearance of a fine sand. Its ground colour was a deep brown, with an admixture of pale or almost colourless particles.

Under a low power of the microscope the individual granules were seen to have a great variety of shapes; some were roughly oval, some oblong or even rod-like, and others, again, were of very irregular outline. Their colour varied from yellow to a warm brown. Some were translucent and others opaque, with the exception of their edges. Some had a finely granular appearance, but none of them showed any indication of crystalline structure (Fig. 1).

Their longest measurements varied between 0·05 and 0·2 mm.

When treated with an acid beneath a cover-glass the particles became surrounded by groups of bubbles, and the solution of the inorganic constituents left exposed an organic basis, brown in colour, wholly structureless, and soluble in alkalies.

No cellular elements could be seen, and the organic basis certainly did not consist of vegetable *débris* of any kind. As in Eichhorst's case, the organic material, when washed with distilled water and stained with methylene blue, was seen to be rich in bacteria, both bacilli and micrococci being present in large numbers.

When, on the other hand, the organic material was got rid of by combustion, the particles of inorganic substance left appeared like decolourised shadows of the original granules, which they resembled both in shape and size.

The air-dried sand lost considerably in weight at 100° C., owing to the expulsion of water from the organic basis, and the percentages of water, organic and inorganic materials contained in it was found to be as follows:

Water	12·40
Organic material . . .	26·29
Inorganic material . . .	61·31
	100·00

The inorganic residue left after combustion over a Bunsen's burner had a bluish-white tint, and contained only a few dark particles. With the exception of such particles, it was completely soluble in hydrochloric acid. This residue was submitted to analysis, and was found to have the following composition:

Calcium oxide (CaO) . . .	54·98
Phosphorus pentoxide (P_2O_5) . .	42·35
Carbon dioxide (CO_2) . . .	2·20
Residue, containing traces of magnesium and iron	0·47
	100·00

The presence of magnesium was beyond doubt, but the quantity was extremely small. Calcium phosphate was clearly the chief mineral constituent.

The pigmentation of the sand proved to be somewhat complex, and the small remainder of the material available did not permit of a complete and satisfactory investigation from this point of view.

When some of the material was treated with acetic acid a scanty evolution of carbon dioxide was observed, and the gas rose to the surface in a stream of minute bubbles. The solution had the colour of brown sherry, and when filtered from the organic *débris* and shaken with ether, it imparted to the ether a delicate pink tint, whereas the subjacent liquid remained of a rich yellow colour. The extraction was repeated several times, and the collected ethereal extracts were next shaken with a small quantity of distilled water, whereupon the pigment left the ether and imparted to the water a rich pink

tint, which recalled that of a solution of acid hæmatoporphyrin.

When examined with the spectroscope this solution showed a broad absorption-band in the neighbourhood of the D line, which lay between

λ6120 and λ5370.

With hydrochloric acid solutions of the pigment the band appeared composite, consisting of two darker bands united by a dark shading, and the position of the component parts was approximately as follows:

First dark band . . .	λ6120—λ5890
Dark shading.	
Second dark band . .	λ5760—λ5460

A second band in the neighbourhood of the F line (λ5060—λ4860) corresponded in position with that shown by a dilute acid solution of urobilin, and was apparently due to a scanty admixture of that pigment.

When kept for a day or two, even in the dark, the pink solution became almost decolourised and the urobilin band alone remained visible. The pink pigment was also promptly decolourised by alkalies.

The very unstable pink colouring matter here present did not agree in its properties with any pigment, fæcal or other, with which we are acquainted.

The yellow liquid from which the pink pigment had been extracted with ether, showed the band of acid urobilin with great intensity, and urobilin was apparently the chief colouring matter of the sand. It had all the ordinary properties of urobilin, as obtained from urine or fæces; was precipitated by saturation of a watery solution with ammonium sulphate; yielded a green fluorescence with zinc chloride and ammonia, and showed the characteristic E-band spectrum when partially precipitated from a concentrated alkaline solution by the cautious addition of an acid.

The organic residue upon the filter-paper acquired a green tint on exposure to air, and when treated with a

solution of sodium hydrate, yielded a pale greenish-yellow solution, which did not become more distinctly green on standing, but which gave Gmelin's reaction. Hence it was evident that among the colouring matters present was a small quantity of unaltered bile-pigment.

Berlioz mentions the presence of urobilin in one of Dieulafoy's specimens, and Eichhorst observed the presence of biliverdin in some granules of the sand which he examined; but the only recorded case in which a special investigation of the contained pigments has been carried out is that of Thomson and Ferguson, who found, in addition to some urobilin, a pigment soluble in dilute hydrochloric acid and in alkalies, but insoluble in water, alcohol, ether and chloroform, and which was obviously not one of the recognised colouring matters of the bile.

We are greatly indebted to Drs. Thomson and Ferguson for the opportunity of examining a small quantity of the sand in question, which in appearance chiefly differs from ours in the larger size of the component granules. From a solution in acetic acid there was not extracted, by shaking with ether, any of the unstable pink pigment above described; and judging by the intensity of the absorption-band the amount of urobilin present appeared to be considerably less than in our specimens.

Varieties of Intestinal Sand.

Although the literature of intestinal sand is so scanty, two distinct classes of materials have clearly been described by this name. These require to be clearly distinguished from each other, and they may be conveniently described as *true* and *false* sand respectively.

1. *False* intestinal sand is composed of remains of vegetable foods which have resisted the action of the digestive fluids, and which may or may not have acquired some incrustation of earthy salts. One particular kind of vegetable *débris* is especially apt to appear as a sand-

like material in the motions, namely, the sclerenchymatous particles which are so abundantly present in the flesh of pears, and especially in that of certain varieties. The occurrence of such sand in the motions was described by C. Robin in 1873, and some at least of the specimens described by Laboulbène in the same year were obviously of this nature. Eichhorst described a case in 1889, and Fürbringer called special attention to this material as simulating biliary concretions. Naunyn also refers to it as one of the varieties of so-called *biliary sand.**

In this country specimens of this kind have been brought before the notice of the Pathological Society of London by Delépine and Shattock.

A specimen of *pear* sand in our possession, for which we are indebted to the kindness of Dr. J. H. Drysdale, is paler in colour and more coarsely granular (0·3—0·6 mm.) than that passed by our patient, and when burnt leaves only 1·76 per cent. of inorganic residue. Other observers have obtained from 2 to 3 per cent. of such residue, figures which contrast sharply with the much higher percentage of mineral constituents in specimens of *true* intestinal sand.

The microscopic appearance of the *pear* sand is very characteristic (Fig. 2). When examined under a low power the granules appear as if studded with projecting crystals, and after removal of any inorganic incrustation by an acid, they are seen to be composed of woody cells, the thick, transparent walls of which are traversed by channels running from the narrow cell-cavities towards the surface. In a word, the granules are easily recognised as identical with the particles of sclerenchymatous tissue in the fruit from which they are derived, and of which the patient will be found to have partaken freely. There is reason to believe that these woody particles may

* Since this paper was read we have found a description of the *pear* sand by Dr. Alexander Marcet, in his "Essay on Calculous Disorders," (p. 132) published in 1817. The description was based upon specimens the true nature of which had been recognised by Wollaston.

remain for some time in the intestine, and the expulsion of large accumulations of them may be preceded by severe colicky pain.

The presence of a black sand-like material in the motions, consisting of cells derived from the banana, has also been described by some American authors. The dark colour is apparently acquired during the passage of the cells along the alimentary canal.

2. *True* intestinal sand, on the other hand, of which the material passed by our patient offers an example, has no such vegetable basis, and, wanting such a rigid skeleton, it owes its hardness and grittiness to the much larger proportion of inorganic material which it contains. The organic basis of such sand is clearly of animal origin. Some of the published analyses of such materials show a very close resemblance to that of our specimen.

Thus Mathieu and Richaud analysed the sand passed by their two patients with the following results:

	Case I.	Case II.
Organic material .	30·800	45·80
Tricalcic phosphate	64·206	46·68
Calcic carbonate .	3·418	5·14
Various mineral substances	1·576	2·38
	100·000	100·00

Thomson and Ferguson's specimen had the following composition:

Organic matter .	28·5
Inorganic matter .	71·5
	100·0
In the inorganic residue:	
Calcic carbonate .	11·7
Tricalcic phosphate	87·3
Insoluble residue (silica) .	1·0
	100·0

Berlioz analysed one of Dieulafoy's specimens and obtained the following figures:

Water	11·25
Nitrogenous organic material of fæcal origin	22·24
Fatty substances	Traces
Phosphoric acid	17·56
Lime	26·22
Magnesia	14·05
Silica	8·68
	100·00

In some other cases the proportion of inorganic material has been considerably less. Thus Marquez found—

Organic matter, of animal origin	72
Inorganic, consisting of calcium phosphate and traces of carbonate	28
	100

In a case recorded by Biaggi, the sand was agglutinated into balls, 6—8 cm. in diameter, which readily disintegrated into sand. Much calcium phosphate was present, with traces of magnesium and sodium.

The material passed in Mongour's case was *gravel* rather than *sand*, and it occupies an intermediate place between intestinal sand and the large intestinal calculi which are sometimes met with, and which are usually composed, in large part, of ammonium magnesium phosphate. Most of the particles were of about the size of an orange pip, but some attained to the dimensions of nuts.

The analysis was as follows:

Organic material (by difference), water, iron	29·28
Magnesium phosphate	26·82
Calcium carbonate	43·90
	100·00

Seat of Formation of "True" Intestinal Sand.

The question remains to be considered how and where sand of this description is formed. Its composition excludes a biliary origin, for it contains no cholesterin, and bile-pigment is only present in traces.

On the other hand, there is much that points to its origin in the intestinal tract. Such sand is practically always met with in association with intestinal disorders, and usually with muco-membranous colitis. The characters of the organic basis, and the large numbers of bacteria which are included in it, point to the intestine as the most likely seat of origin.

When our patient was taking bismuth salicylate the sand passed had a uniform grey tint, but this may have been due to the deposition of a mere surface coating of bismuth sulphide.

The richness of the material in urobilin and its poverty in unaltered bile-pigment affords a more satisfactory indication, and suggests that it is formed in a region in which the conversion of the bile-pigment into urobilin is already far advanced. There is good reason to believe that the principal seat of this change is in the upper regions of the colon.

Concretions, chiefly composed of calcium phosphate and carbonate, can hardly be formed in any but alkaline surroundings; but there is so much doubt as to the reaction of the contents of different parts of the intestinal tract, and especially under morbid conditions, that this does not afford any very clear indication of the exact locality in which the sand is formed.

The nature of the inorganic constituents is fully compatible with an intestinal origin. Nor is it necessary to look to unabsorbed residues of the calcium of the food as the sole source of supply, for Voit, Friedrich Müller, and von Limberg have shown that a large part of the calcium excretion of the body is effected by the intestine, and

Kobert and Koch found calcium, magnesium, and phosphoric acid in the material which accumulated in the empty and cleansed colon of a patient with a fæcal fistula.

Like Thomson and Ferguson's patient, ours had taken milk and lime-water freely, and, as Bunge has shown, the amount of lime contained in milk is actually greater than that present in an equal volume of lime-water; so that the former may be regarded as a more important source of calcium supply than the latter.

The above considerations leave little room for doubt that true intestinal sand has its origin in the intestinal canal, for chemical and clinical evidence alike point in this direction. The nature of the contained pigments suggests the colon as the most likely seat of formation, and the anatomical structure of the large bowel may be looked upon as more favourable than that of the small intestine to the sojourn required for the deposition of the earthy salts of which the material is so largely composed.

Bibliography.

Bates, K. L.—Intestinal Concretions resembling Sand, and originating in Cells from the Banana. Amer. Journ. of Med. Sci., 1887, xliii, p. 441.

Biaggi.—Du sable intestinal. Presse Médicale, Belge, 1874, xxvi, p. 153.

Delépine, S.—Sable Intestinal and some other Intestinal Concretions. Trans. Path. Soc., London, 1890, xli, p. 111.

Dieulafoy, G.—Lithiase intestinale et entéro-colite sableuse. Clin. Méd. de l'Hôtel Dieu, Paris, 1896–97, p. 273.

Dieulafoy, G.—La Lithiase intestinale et la gravelle de l'intestin. Bull. de l'Acad. de Méd., Paris, 1897.

Edes.—Appearance of Altered Banana in the Dejections. Boston Med. and Surg. Journ., 1883, cviii, p. 446.

EICHHORST.—Lehrbuch der physikalischen Untersuchungs-Methoden, 1889, 3te Aufl., p. 240. Specielle Pathologie und Therapie, 1895, 5te Aufl., ii, p. 414. Ueber Darmgries. Deutsches Arch. f. klin. Med., 1900, lxviii, p. 1.

FÜRBRINGER, P.—Zur Kenntniss der Pseudogallensteine. Verhandlungen des Congresses f. innere Medicin, 1892, xi, p. 313.

JONES, E. C.—A Case of Muco-membranous Colitis, with Deposit of Intestinal Sand. Medical News, 1897, lxx, p. 120.

LABOULBÈNE.—Sur le sable intestinal. Arch. générales de Méd., 1873, 6e s., xxii, p. 641. Bull. de l'Acad. de Méd., Paris, 1893, 2e s., ii, p. 1383. Nouveaux éléments de l'Anat. path., 1879, p. 231.

LANGENHAGEN, M. DE.—L'entéro-colite muco-membraneuse. Semaine Médicale, 1898, xviii, p. 4.

MARQUEZ.—Note sur le sable intestinal. C. R. de l'Assoc. Française pour l'Avancement des Sci., 1879, p. 878.

MATHIEU, A., et RICHAUD, A.—Deux cas de sable intestinal et d'entérite muco-membraneuse. Bull. et Mém. Soc. Méd. des Hôpitaux, Paris, 1896, 3e s., xiii, p. 473.

MATHIEU, A.—Sable intestinal en dehors de l'entérite muco-membraneuse. Bull et Mém. Soc. Méd. des Hôpitaux, Paris, 1897, 3e s., xiv, p. 513.

MAZERAN, A.—Calculs de l'intestin et gravelle intestinale. Thèse de Lyon, 1899, p. 53.

MAZERAN, A.—La gravelle intestinale. Revue Internat. de Médecine et de Chirurgie, 1899, Sept. 25th.

MONGOUR.—Note sur un cas de lithiase intestinale. C. R. de la Soc. de Biologie, Paris, 1896, p. 203.

NAUNYN.—Klinik des Cholelithiasis, 1892, p. 79.

ODDO.—Sable intestinal. Bull. et Mém. de la Soc. Méd. des Hôpitaux, Paris, 1896, 3e s., xiii, p. 539.

ROBIN, C.—Dictionnaire de Nysten, 1873, 13e édit., p. 1226.

SHATTOCK.—Sable intestinal. Trans. Path. Soc., London, 1897, xlviii, p. 124.

THOMAS, D.—Australasian Med. Gaz., 1891–92, xi, p. 56.

THOMSON, R. S.—Glasgow Med. Journ., 1898, xlix, p. 202.

THOMSON and FERGUSON.—An Analysis of Sandy Matter (Sable Intestinal) from the Human Intestine, with special reference to a contained pigment of unusual character. Journ. of Path. and Bact., 1900, vi, p. 334.

DISCUSSION.

Dr. CROMBIE.—I think the occurrence of intestinal sand must be more frequent in India than it appears to be in this country. During the last ten years of my service in India as Superintendent of the European General Hospital, Calcutta, I saw three cases of the kind. The patients were between twenty-five and thirty-five years of age. The chief symptom was colic, sometimes intense and severe, but not continuous. There were intervals when there was little or no colic, followed by paroxysmal attacks. Intestinal sand exactly like that shown here to-night, but of rather coarser grain, was found in the motions whenever these were examined, the quantity being greatest when the pain was most intense. It may be that one reason why we meet with these cases in India more frequently than is done here is the fact that it is part of the daily routine of Indian hospitals to examine the motions in all cases whenever intestinal symptoms of any kind exist. There is one point which I mention with a certain amount of diffidence, but I feel that when a disease is as obscure as this is, every point should be noticed, however extraordinary it may appear. One day, when examining some sand microscopically with a low power, I was surprised to find that there was moving in it an acarus. I looked upon its presence as accidental, but, six months later, on examining a specimen from my second case, I again found an acarus present, which I captured and submitted to the Superintendent of the Indian Museum for identification. He said it was an immature acarus of a kind with which he was not acquainted. Some time later a colleague of mine secured a specimen of sand from a third patient in another part of the hospital, and on examining it microscopically found a living acarus present. There was a fourth individual at the hospital with intestinal sand, in the person of a pig, which I proposed to feed with the motions of my second patient by way of experiment; but on examining the pig's motions, as a preliminary precaution, I found that the animal was also passing intestinal sand. With regard to the presence of acari in the intestinal sand in specimens from each of the three cases which were observed by myself and my colleague, I should mention that acari were never seen except in these cases, and it must therefore be acknowledged that their presence, if accidental, was extremely remarkable.

Mr. BOKENHAM.—I was recently asked to examine the washings from the stools of a patient who presented symptoms resembling those of biliary colic. The patient, a somewhat

neurotic lady, thirty-two years old, had periodic attacks of colicky pain, with much flatulent distension of the abdomen, and free motions. These motions for some days after an attack deposited a greater or smaller amount of heavy, dark brown, sandy matter, which the doctor in attendance thought to be fragments of gall-stones. I am able to show specimens of this sand to the Society, both in the dried and incinerated forms, and would point out that to the naked eye it very closely resembles the sand from the case of Drs. Thomson and Ferguson. Chemically I find that the sand consists of over 60 per cent. of inorganic matter, principally calcium phosphate, the remainder being organic matter. Unlike the residue in the other cases, it seems to contain practically no calcium carbonate, as no effervescence occurs when a specimen is treated with an acid. I have applied most of the tests enumerated by Dr. Garrod, and have been able to detect the following points of difference and resemblance:—(1) There is absolutely no cholesterin present, therefore the diagnosis of gall-stones is negatived; (2) I was unable to extract with ether from an acetic acid solution of the sand any pink pigment, such as described by Dr. Garrod; (3) both the acetic acid and hydrochloric acid extracts gave the characteristic absorption spectrum of urobilin; (4) a certain proportion of the sand is insoluble in hydrochloric acid, but soluble in alkalies. The application of Gmelin's test to this residue reveals the presence of only minute traces of bile pigment. I think the whole evidence goes to show that this sand is formed, not in the acid jejunum, but much lower down in the intestinal tract, possibly in the neighbourhood of the appendix. That the condition is a rare one I am convinced. I have had to examine a number of stools every week for some years past, and this is the first instance in which I have found anything at all resembling intestinal sand. I feel fortunate in being able to make this brief addition to the number of recorded cases.

Sir Dyce Duckworth.—Cases of this disorder are so rare that we could hardly expect the subject to give rise to much discussion. Dr. Crombie's experience is certainly interesting, but so far as I am acquainted with the literature of the subject I was not aware that cases of enteric sand were common in India. We hope our contribution may arouse attention to this symptom and so lead to a more careful examination of the stools of patients suffering from diseases of all kinds. I am afraid that in this country we are less careful than they are on the Continent in this respect, as is evident from the perusal of their clinical notes and observations. We examine the stools in enteric fever or colitis, or in other obvious intestinal affections, but I think our knowledge of the possible relations of enteric

sand to these conditions should lead us to examine the stools in all cases where colic is complained of, since most of these cases present colicky symptoms. Such colic has often been attributed to biliary or renal gravel, especially in cases in which none has been passed. Most of us can recall cases of this kind. The sand is readily detected on the addition of a little water when it falls to the bottom of the vase. A study of the motions day by day reveals drachms of this sand, and one wonders where it is produced. This goes on for weeks or months, then gets less, then finally ceases altogether. Dr. Garrod's researches point to the probability of its formation in the upper part of the colon where it is stained by pigments also formed in that region. Its presence appears to give rise to much pain and flatulency with periodical attacks of severe distension. The general health suffers, the patients lose flesh and become anæmic. The subjects of the disorder are often neurotic, *i. e.* persons whose nervous system is unstable and excitable. The connection with gout is uncertain. In this case there was an unequivocal history of gout in the father, and in one of the other children there was the alternation of eczema and asthma. The great point in treatment appears to be to restore the patients to a better state of health by careful dieting and by the use of astringents, bismuth, etc. Relapses may occur, and no doubt such patients require to be particularly careful in regard to diet, especially as to vegetable food. The sequels of such cases will always be interesting, and I shall endeavour to follow up this instance and to discover whether any relapse or other symptoms occur. I may add that the last accounts of this patient are quite satisfactory. No sand is now passed, the general health and digestive capacity have improved, and there has been continuous gain in weight.

Dr. Garrod.—The unstable pink pigment appears to be a special feature of the sand passed in the case described, seeing that it was not present in the specimen sent by Drs. Thomson and Ferguson, nor in that examined by Mr. Bokenham. In the post-mortem room I have never met with any condition of the intestine which appeared to throw light upon the mode of origin of intestinal sand.

FIG. 1.

True intestinal sand, from the case described.

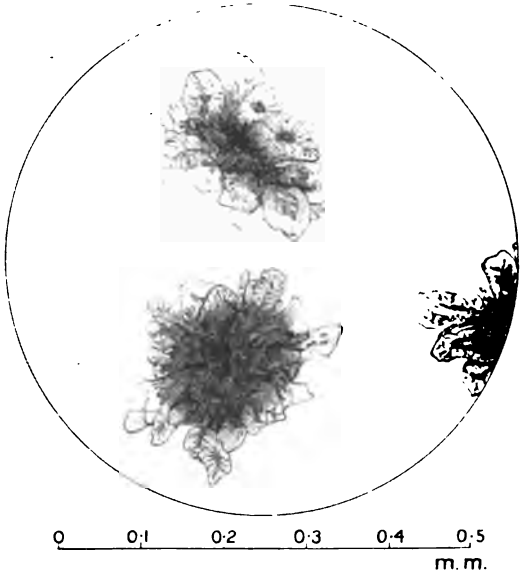

FIG. 2.

False intestinal sand, consisting of sclerenchymatous particles of pears.

Bale & Danielsson, Ltd., Lith.

AN ACCOUNT

OF THE

EPIDEMIC OUTBREAK OF ARSENICAL POISONING

OCCURRING IN

BEER DRINKERS IN THE NORTH OF ENGLAND AND THE MIDLAND COUNTIES IN 1900

BY

ERNEST SEPTIMUS REYNOLDS, M.D., F.R.C.P.Lond.

ASSISTANT PHYSICIAN TO THE MANCHESTER ROYAL INFIRMARY; VISITING PHYSICIAN TO THE MANCHESTER WORKHOUSE INFIRMARY

Read January 8th, 1901

For the last twelve months I noticed, both in the medical wards of the Manchester Workhouse Infirmary and in the out-patient department of the Manchester Royal Infirmary, a considerable number of cases presenting unusual skin eruptions of a more or less indefinite character, such as erythema, keratosis, and pigmentation,

the last being particularly common among the pauper patients. Some of the pigmented cases were diagnosed as Addison's disease by my assistants, but I could never satisfy myself that this diagnosis was correct. In June, 1900, about six patients presented themselves in one week who were suffering from the typical erythromelalgia or painful red neuralgia of Weir Mitchell, not only the feet but in some cases the hands also being affected; so marked were these cases that in June I gave a clinical lecture on the condition to the students of the Manchester Royal Infirmary. During the last seven months, I noticed a remarkable increase in the number of cases of herpes zoster, which appeared to be in epidemic form, and during this period I saw probably more cases than I had seen altogether in the past two years.

At the beginning of August quite an extraordinary number of cases of so-called "alcoholic paralysis" were admitted into the workhouse hospital, principally among women. So-called alcoholic peripheral neuritis is a fairly common disease in the Manchester district, very much more common as I understand than in London and the south, and perhaps I may be excused for saying that we are specially well acquainted with the affection, for it was principally owing to the work of our physicians Dr. Dreschfeld and the late Dr. J. Ross, that such excellent descriptions were given to the medical world. By it we understand a peripheral neuritis associated with paræsthesiæ and numbness in the hands and feet, paralysis of the arms and legs, cramps of the muscles, and especially great pain on pressure of the muscular masses of the limbs; in addition there is frequently a dilated left heart with cardiac muscle failure, and marked œdema of the trunk and legs and often albuminuria; very rarely indeed, almost never, is there any affection of the cranial nerves. In some cases there is an almost characteristic mental condition with loss of memory for time and place. It may be at once mentioned that the only forms of peripheral neuritis associated with great pain on muscular

pressure are, the alcoholic,[1] the arsenical, and that form found in beri-beri.

This great increase in the number of cases of alcoholic neuritis was noted by many observers, some of whom thought that it was due to increased drinking, owing to the war fever, or to a wrongful expenditure of the money given by the charitable towards the war funds. There was at the beginning of November no longer any doubt that a serious epidemic existed not only in Manchester and Salford, but also in neighbouring towns. Now, rightly or wrongly,—and this is a matter far too large and important to discuss in this paper,—I have for many years doubted whether ethylic alcohol *per se* does cause peripheral neuritis at all, and I have personally felt more confirmed in this opinion each succeeding year. I was therefore, in the present epidemic, not content with the alcoholic theory, but was at once on the look-out for some other possible cause of the neuritis. I could not at first find a satisfactory explanation, but at any rate I confirmed a previous opinion,[2] that in this district alcoholic neuritis only occurred among beer drinkers, not amongst pure spirit drinkers. Then we noticed at the workhouse, that the peculiar skin lesions already mentioned in passing were very often found in the patients who were suffering from neuritis; secondly a few cases of beautiful herpes zoster were found in the neuritic cases. Thereupon I remembered that arsenic was the only known drug which produced herpes, and so if there was any known drug acting as a poison in the beer it was almost certainly arsenic.

Improbable as this hypothesis at first seemed, yet it was a valid hypothesis, for it was not known to be untrue, it explained all the facts, and it was easily capable of proof or disproof. This hypothesis I imagined on November 15th, 1900. On November 17th I obtained some of the beer most commonly partaken of by the

[1] By "alcohol paralysis" or neuritis in this paper I mean *so-called* alcoholic paralysis or neuritis.

[2] See 'Medical Chronicle,' June, 1890, p. 189.

sufferers, and on November 18th, by Reinsch's test, I easily obtained a deposit on the copper foil, and driving this off in a combustion tube, I got well-marked crystals of arsenious oxide, and thus the hypothesis became a fact.

Source of the arsenic.—On speaking to Dr. H. A. G. Brooke about the skin lesions he told me that he was treating a young London hop merchant for similar eruptions, and by his kindness I saw the patient with him, and we found that he had undoubtedly got slight arsenical poisoning, although he took very little beer; but he frequently chewed hops, and we concluded that the sulphur with which the hops were treated would be found to be the source of the arsenic. This was soon found, however, not to be the cause of the present epidemic, especially as so little hops are used in making cheap beers. I have, however, been informed that the sulphur is often contaminated with arsenic, and in this way hops on the market often yield a reaction showing the presence of traces of arsenic, thus accounting for the symptoms in a gentleman constantly tasting them. I communicated my discovery of the arsenic to Professor Dixon Mann on November 19th, and on November 20th he examined a different sample of beer and also found arsenic. He informed Professor S. Delépine, who was, unknown to me, also investigating the epidemic at the request of Mr. C. H. Tattersall, the medical officer of health of Salford, and he, on November 22nd, traced the arsenic to certain sugars used in brewing. These were invert sugar, made by the action of sulphuric acid on cane sugar, and glucose, made by the action of sulphuric acid on various forms of starch. It was easy to see that the sulphuric acid was the common source of the arsenic, and on being examined large quantities were found, the original source being the Spanish pyrites from which the sulphuric acid is made, and which often contains a very large percentage of arsenic. As it happened, the brewing sugars from one firm only were found to be thus

contaminated, but as this firm supplies no less than 200 breweries in the North of England and Midland Counties, it will be seen how wide-spread the epidemic was likely to be.

Quantitative analyses.—By the kindness of Professor Delépine, I am able to give some interesting quantitative determinations, the arsenic being estimated as arsenious oxide. Various beers were found to contain from two to over four parts per million, that is from 0·14 to 0·8 grain per gallon. The invert sugar contained 0·25 part per 1000, the glucose 0·8 part per thousand, and the sulphuric acid no less than 1·4 per cent., or four ounces per gallon.

Other sources of arsenic.—From a legal and commercial point of view these results are of the highest importance, but from a scientific point of view it is equally important to know that traces of arsenic may get into beer from other sources. I have already mentioned that it is contained in sulphured hops; it is also found in many samples of malt, getting there either from sulphur or from anthracite coal; it has been found by Dr. John Brown, of Bacup, in the vulcanite tubing used for conveying the beer to the pumps. Again, calcium bisulphate and sulphuric acid are used in "fining" the beer, and also, I believe, for cleansing the barrels. Another point worth recording is that many artificial manures are contaminated with arsenic. A possible explanation of the manner in which arsenic may be retained in beer during the various processes, and may be of peculiar virulence, is that, according to the researches of Selmi, Hamberg, Sanger, Saccardo and others,[1] certain micro-organisms, especially *Aspergillum glaucum*, *Mucor mucedo*, and *Penicillium brevicaule*, seem to have a special tendency to seize hold of any arsenic in their vicinity, and to manufacture specially poisonous arsenical products. This has so far been worked out more particularly in connection

[1] Allbutt's 'System of Medicine,' vol. ii, p. 989.

with arsenical wall papers, but, as Dr. R. T. Williamson [1] points out, it is very desirable that further researches on these arsenio-bacteria should be made.

Extent of the epidemic.—Although the epidemic seems to have fallen most heavily on Manchester and Salford, and the vicinity, yet many more distant towns in the North of England and the Midlands have been affected,—wherever indeed the contaminated brewing sugars were used. Thus we hear of outbreaks in Liverpool, Chester (where the cases were associated with so much heart failure and so little pigmentation that they were diagnosed as beri-beri), Warrington, Heywood, Bacup, Preston, Lancaster, Penrith, Ilkley, Leicester, Stourbridge, Lichfield, and Darleston.

Although very many thousands of people have probably been affected, yet it is impossible to say how many, and equally impossible to give the number of deaths. For the epidemic had been in existence for nearly six months before anything except alcohol was suspected as the cause; many cases were treated as rheumatism, others as gastritis or diarrhœa, large numbers simply for the skin eruptions, and many merely as cases of chronic alcoholism. Some patients only had slight symptoms, and did not have medical attention, while in others the cardiac and hepatic symptoms were the important features.

But some idea may be obtained from certain statistics obtained by Dr. J. Niven, Medical Officer of Health of Manchester, and Mr. Tattersall, Medical Officer of Health of Salford. The former, in response to a circular received information from ninety practitioners, and came to the conclusion that there had been up to the end of November in Manchester only at least 2000 cases. Investigating his death tables and including deaths certified as due to neuritis, alcoholism, or cirrhosis of the liver, for the first ten months of the years 1897, 1898, 1899, and 1900, he found them to amount to 172, 141, 188, and 253 respectively. In Salford, Mr. Tattersall found that

[1] 'Brit. Med. Journ.,' December 1st, 1900.

in the four months from the end of July to the end of November, 1900, there were forty-one cases of death certified as due to neuritis, and twenty-five as due to alcoholism; this total of sixty-six contrasted with twenty-two in the first seven months of the year, thirty-nine in the whole of 1899, thirty-one in 1898, and twenty-seven in 1897.

Symptomatology.

1. *Complaint of patient.*—In answer to the usual question, "What is the matter with you?" the patients have complained of one or more of the following symptoms:—pains in the feet, hands, and limbs, burning in the soles of the feet, tingling, and "pins and needles" in the fingers and toes, shooting neuralgic pains in the trunk and limbs, difficulty of walking, weakness in the hands and legs, rashes on the body, frontal headache, running of the eyes and nose (cold in the head), bronchitis and hoarseness, a "tired-out" feeling, shortness of breath, swelling of the feet, vomiting, and diarrhœa.

2. *Aspect.*—The aspect of most of the patients is so typical that their cases can generally be diagnosed at sight, not only as they come into the out-patient room, or lie in bed, but as they walk about the streets of the city. The face is puffy, especially about the eyelids. The eyes are suffused and watery, and sometimes running with tears; in some cases the conjunctivæ being œdematous, and the vessels so congested that at first sight there appear to be subconjunctival hæmorrhages. The colour of the face varies from crimson to a dusky red, or even a copper colour. The voice is often "husky," sometimes intensely so, and the walk is that of a patient with very sore feet, so that they seem afraid to put the foot to the ground; or it is somewhat unsteady; or else there is the "high-stepping" gait from paralysis of the dorsal flexors of the ankle. In many cases the gait can be diagnosed merely by the noise of the footfall on the ground—the

"double-rap" step as I call it,—the heel coming down first, quickly followed by a sudden (not gradual as in health) descent of the anterior part of the foot, and so making the second rap. The patients very frequently are found to be rubbing the fingers together because of the numbness and tingling.

3. *The skin lesions.*—These are very numerous, and almost invariably present in some form or another in greater or lesser degree. (*a*) Erythromelalgia.—This condition, described as "painful red neuralgia of the extremities" by Weir Mitchell, or "acrodynia" by older observers, was one of the commonest lesions. The soles of the feet are crimson, as if stained with red ink, sometimes the whole surface, but more generally only where the surface touches the ground, so that there is left a normal appearance on the inner side at the hollow of the foot, and also a transverse line just beyond the distal extremities of the metatarsal bones. The sole and often the whole foot is bathed in perspiration, which may be stinking (but this is rare). The skin is also puffy, even if no true dropsy is present. On the palm the redness may, again, be uniform; but, again, more frequently it is most marked on the thenar and hypothenar eminences, and on the palmar surfaces of the terminal phalanges, the centre of the palm being normal in colour; the whole palm is wet, and may be actually pouring with sweat. Both soles and palms are tingling and burning hot, and painful, and these signs are greatly intensified by heat, so that the patient cannot sleep unless the feet are exposed to the air outside the bed-clothes.[1] The pressure of the bed-clothes cannot be borne, and the surfaces are exquisitely painful on pressure, so that, as I have said, the gait is affected, and the patients cannot use the hands even if no paralysis is present. This erythema does not become pigmented, but passes on to keratosis. (*b*) Keratosis.—This condition seems to be a somewhat late mani-

[1] Rarely the patient says his feet are very cold, but on examination they are proved to be hot.

festation, and is, at any rate, very frequently secondary to the erythema and hyperidrosis of the palms and of the soles. I have watched it develop on the hands and feet, and can thus speak with some certainty. It may take several forms; it may be in a few isolated scaly masses, either thin or very heaped up in marked prominences, and in this way previous corns on the feet, or patches of tylosis on the soles or palms become extraordinarily prominent. In some cases the keratomatous patches appear on the dorsum of the hand, between the webs of the fingers, and on the knuckles. In more marked cases, either the whole palm or sole is thickly covered with large white or dirty grey scales, which are constantly being shed into the bed-clothes; or the centre of the palm and inner side of the sole may be merely erythematous and dry, but not covered by scales. Sometimes the keratosis extends up to the ankles and on to the wrists, but the scales are now not thick, but more like a brawny desquamation. The palms and soles may both be affected, but the soles are almost always the worst, and sometimes are affected alone. Moreover, in cases where there is no pigmentation, keratosis may be present, and forms a most valuable aid in the diagnosis of a case which might otherwise appear to be merely one of alcoholic paralysis. The process is very slow (many weeks) in its development, and seems to be, if untreated, extremely chronic. (*c*) Erythemata.—These are very varied in character, and are often accompanied by great irritation. There is sometimes a scarlatiniform eruption on the upper part of the chest spreading to the neck and face, sometimes on the forearms and rest of the body. At other times, and perhaps more frequently, it is amorbilliform rash on the trunk and limbs, running into scarlatiniform patches; often it is a more distinctly papular erythema, and not unfrequently there is an acute urticaria. In some the change is so intense that there is a vesicular eruption, in which the lesions may vary in size from that of a pin's head to large bullæ several inches in diameter. Those I have seen have been almost always on the limbs.

In one or two cases the appearance has been that of a true pemphigus, and when the contents have been shed circular marks have remained, like very superficial scars. These vesicular eruptions are probably a late form of rash. even coming on six weeks after the last glass of beer has been taken. The erythematous papules sometimes become larger, run together, and are covered with scabs in patches, so that there may be after many weeks an appearance somewhat like lupus, or even of syphilitic superficial ulcerations. (*d*) Pigmentation.—This is generally not present in light-complexioned patients, or merely amounts to a darkening of pre-existing freckles. In darker people it is practically always present in greater or less degree, but in many is so diffuse that it may entirely escape notice. In most of the cases it follows on (after many weeks) the erythematous blush, which gradually turns from red to copper-colour, then to bronze, and in severe cases almost to black, so that many of the cases resemble mulattoes. Even if it is thus almost universal, it does not affect the palms and soles, nor as a rule does it touch old scars in which the deeper layers of the skin have been destroyed; but round the edge of the scar it is much intensified, the scar thus seeming of an especially white character. Round the neck, in the armpits, round the nipples, on the abdomen, round the genitals, and on the buttocks, where there has been pressure, as round the waist, or under the garters, it is much deeper in tint, and indeed resembles the pigmentation of Addison's disease; but I have not seen any pigmentation of the mucous membrane of the mouth. Although well seen on the face of many patients, yet on the whole it is more marked on the trunk. Frequently the pigmentation shows well-marked lighter spots, like "rain drops." In other cases the pigmentatation is seen on close examination to be punctiform. In others it is in isolated spots varying in size from a pin head to patches equal in size to the palm of the hand, clear light-coloured skin intervening, and often these isolated patches run together to form a con-

tinuous pigmentation. Not only is the colour like that of a mulatto, but the texture of the skin takes on the same beautifully soft velvety feel to the touch, quite different from that of normal English skin. In many cases, after many weeks a branny desquamation of the pigmented skin takes place, so that by friction one can rub off the pigmentation, as it were, and leave healthy skin underneath. Having watched numbers of these cases for weeks, I am convinced that there is a distinct sequence of events, namely an erythema followed by pigmentation, and then a desquamation, so that the pigment is really a part of the general altered nutrition of the skin and is not due to a deposit of metallic arsenic in the skin, as was once thought; this view does not necessarily exclude the idea that the drug may be partly eliminated by the skin.

(*e*) Herpes zoster.—This was the tell-tale eruption which, as I have said, gave me the key to the puzzle. When it occurred without any other very definite symptoms, then I considered I was dealing with epidemic specific herpes, but when I found other signs of arsenic poisoning present, there could be no doubt that it was also arsenical in origin. Since the discovery of the arsenic, practically every case of herpes zoster has been found to have other unmistakable signs of arsenic poisoning in greater or less degree. I have seen rarely herpes of the fifth cranial nerve, a few cases of the ascending branches of the cervical plexus, several of the other cervical nerves, many of the dorsal nerves, and one of the first lumbar nerve. In no case has the herpes been bilateral, and generally only one nerve-root was affected; but in two cases I have seen two succeeding nerve-roots affected; I have seen no herpes below the elbow or below the knee. From the great number of cases seen in this district, there is to my mind no longer any doubt that arsenic causes herpes by a direct action on the posterior spinal ganglion, just as much as it acts directly on the motor and sensory nerve-fibres. This seems to me to be a much more probable view than that put forward by Dr. H. Head, that

arsenic is only a remote cause of herpes, inasmuch as it renders a person more liable to attack by specific herpes. In fact how many of the epidemics of so-called specific herpes (such as that described by Dr. Head as occurring in 1897, during the long drought that lasted from July to November) have not really been due to arsenical poisoning? From actual therapeutical observation, I have seen a few cases of herpes develop when I have been giving small doses of arsenic in which the only other sign of arsenical poisoning was lachrymation and a silvery tongue. I am, indeed convinced, that it may come on with quite small doses. The herpetic eruptions have always been preceded and accompanied by very severe neuralgic pains along the course of the nerve or nerves affected. And I may here state that I have had many cases with severe neuralgic pains in the arms or round one side of the trunk which I expected would be followed by herpes, but none appeared. (*f*) Nails.—In many cases the nails are affected. After the patients have stopped taking the beer for some weeks the best appearances are seen, for then there is a transverse white ridge across the nail; proximal to this the nail is normal, but distal to it the nail is whiter, cracked, thin, and towards the tip almost papery and much flattened. In some cases there have been a series of parallel transverse ridges of the nails, also suggesting a series of week-end "drinking bouts." These deformed nails of course break easily. (*g*) Loss of hair.—One or two women have told me that they have lost the hair during the attack, but this has certainly not been a marked feature.

4. *Nervous system.*—(*a*) Sensory affections have been present in practically all the cases. In the mildest they have merely consisted of paræsthesia and tinglings, and burning and pricking sensations in the fingers and toes; in others this has been combined with numbness of the hands and feet, and sometimes of the legs below the knees. I have not seen a case of *total* loss of sensation, although the numbness has been very pronounced. Part

of the apparent loss of power in the hands and feet has been due to this partial loss of sensation. In one case there was very marked, but not total, anæsthesia of the whole left fifth cranial nerve, but its motor fibres were unaffected. This is the only instance in which I have seen any affection, either sensory or motor, of the cranial nerves. Neuralgia of the arms or trunk, either followed or not by herpes, I have already alluded to. Finally, and of the greatest diagnostic importance, there was in a large number of the cases (but only if there was some loss of power) tenderness on pressure of the muscular masses of the legs and arms; sometimes deep pressure was required, but in other cases light pressure produced most exquisite pain, and caused the patients to scream out, and to exhibit a very typical facial expression of terror, or in less marked cases merely a screwing up of the facial muscles in a "grin of pain." (*b*) Motor: These symptoms were similar to those ordinarily found in so-called alcoholic neuritis. They were present in greater or less degree in about 70 per cent. of the cases. In the slighter cases there was only slight loss of grip and slight affection of the gait, and there was then no appreciable atrophy of the muscles. In more marked cases there was a total paralysis of the affected muscles, with very marked atrophy. The small muscles of the hands, especially the interossei; the muscles of the forearms, especially the extensors; and in severe cases all the muscles of the arm were involved. If the muscles of the upper arm were not affected, then also the supinator longus escaped to a large extent, as in lead poisoning. In the early stages in the feet there was loss of power with some slight irritation of the extensors of the toes, so that the great toe was well extended and "cocked up." In this stage the knee-jerk was always either present or exaggerated, but there was never any ankle clonus. But soon the muscles became paralysed and atrophied; first the interossei and the anterior tibial and peroneal groups, so that the toes were flexed, and the whole foot dropped

at the ankle into a position of talipes equino-varus. The calf muscles were next affected, and at about the same time those of the thigh, accompanied, of course, with rapid wasting and loss of the knee-jerks. The superficial reflexes were normal or exaggerated. Even in this stage the muscles on the front of the trunk were weak, so that the patients could not raise themselves in bed, and in some advanced cases there was well-marked diaphragmatic paralysis, with laboured breathing and a markedly ineffective power to cough. In one case, with comparatively slight loss of power in the limbs, the diaphragm was entirely paralysed. It goes without saying that in the most advanced cases the patients lay in bed totally helpless. There was no paralysis of the sphincters, except in the most marked cases, in which some of the incontinence was possibly due to the mental condition, and the intercostal muscles were never paralysed. I never saw any paralysis of the cranial nerves in any case. The walk I have already described as the "stepping" gait, but many of the patients were distinctly incoordinate in their movements, and swayed slightly on standing with the eyes closed, but to my mind there was never any real resemblance to the ataxic walk of a case of tabes. (*c*) Mental: In many of the cases of advanced paralysis there was the peculiar mental condition commonly found in alcoholic paralysis. This has been called confusional insanity, but it is more accurately described as a total loss of memory of time and then of place. There is a loss of initiation of ideas, but any suggestion, however absurd, is at once accepted. Thus a totally paralysed patient, who has been in bed for weeks, when asked if he has not been for a walk this morning, will say that he has, and will tell you with much circumstance where he has been; and when asked about yesterday, will perhaps say, with a little prompting, that he has been to the seaside. If asked when he came into hospital, he will always turn towards the nurse at the other side of the bed and say, "Let me see, I think it was

yesterday [or some other near date], wasn't it, nurse?" But taking only the paralysed cases, I am inclined to think that the amount of mental confusion has been distinctly less than I should have expected from as many cases of ordinary alcoholic paralysis, which rather leads me to think that arsenic has not much effect on the cerebral cortex.

5. *Circulatory system.*—In the majority of the patients there has been some heart failure. In the milder cases this has been limited to dyspnœa on slight exertion, palpitations, post-sternal or epigastric pain, and a low tension pulse. In more marked cases the heart muscle has shown great failure, and the left side of the heart has been dilated, the apex beat has been in or outside the nipple-line and the left border not infrequently outside the nipple-line; the beat was sometimes diffuse. On auscultation the heart-sounds have approached the fœtal "tic-tac" type, the second sound being accentuated, and the diastole shortened to the length of the systole; in some cases there was a soft systolic mitral murmur. Exertion has increased the pulse rate considerably, and there has sometimes been a rapid heart without accompanying fever. So great has been the cardiac muscle failure that several patients have fainted on getting up for the first time, and undoubtedly the principal cause of death has been cardiac failure; this has been noticed as the chief cause of death in arsenical poisoning by Brouardel in the Havre epidemic in 1888 (homicidal poisoning). Œdema affecting merely the feet only or almost the whole body has been observed in 25 per cent. of the cases. On the trunk it may manifest itself by the skin taking and retaining the impression of the stethoscope over the heart. There is often a well-marked pad of œdema over the sacrum, and the genitals are sometimes enormously œdematous. The legs may have such a tense hard œdema that it is difficult to make an impression on them with the finger. There has been a fair amount of ascites, but no great amount of peri-

cardial or pleuritic effusion, certainly not so much as is said to occur in beri-beri. In the Chester cases there seems to have been an unusual amount of heart failure and œdema. Both from the cases which I have seen and from those reported in other epidemics I have no doubt that arsenic will seriously affect the heart muscle quite independently of alcohol.

6. *Respiration.*—Just as the skin is irritated by the arsenic so the respiratory mucous membrane seems to be in its whole course. There are in the early stage running from the eyes and nose, congestion of the fauces; a very marked congestion and thickening of the vocal cords producing the typical hoarse or husky voice (not due to any paralysis, as I have proved by laryngoscopic examination) and very pronounced bronchitis. Not infrequently there has been hæmoptysis in patients who were certainly not suffering from phthisis. Not a few of my cases have shown signs of phthisis with fairly rapid breaking down of the lung tissue. And it is interesting to note at the present time, when arsenic is being largely recommended for the treatment of phthisis, that some of our patients with signs of rapid phthisis give a history of apparently previous phthisis which has seemed to be in abeyance but has been lighted up in a virulent form by drinking the arsenicated beer.

7. *Digestive system.*—In many of the cases digestive troubles were the first signs; although loss of appetite was present in severe gastric cases, on the contrary in mild cases the appetite seems to have been definitely increased. There was, of course, no blue line on the gums in any case, but in a few the gums were red and softened. The tongue in the early stage had a typical thin white silvery coat, as if it had been brushed over with lunar caustic. In later severe stages it was brown, but as a rule it was moist. Vomiting quite sudden and very copious was a marked feature, sometimes occurring immediately after each pint of beer taken, or immediately after a meal. Many patients came to the hospital suffering from

sensory disturbances and said that they were spirit drinkers only, but on inquiry I found that they had been beer-drinkers a few weeks previously, but had voluntarily stopped the beer because it was not "agreeing" with them, as they were so sick; and this occurred before it was known that arsenic was present in the beer. Some cases complained of diarrhœa, and as these cases occurred in October and November, I was quite at a loss to explain the cause, especially as they had not as yet other signs of arsenical poisoning, although they were obviously alcoholics. In a few cases there has been passing of blood by the stool, but whether this was secondary to congestion of the liver or to ulceration of the intestine I cannot say. At the workhouse hospital during the last six months we have had quite an unusual number of cases of cirrhosis of the liver (this organ being much enlarged, hard, and tender) with great ascites. Dr. Sturrock, the resident medical officer at the Manchester Royal Infirmary, has noticed the same increase there.[1] Brouardel has also mentioned cirrhosis of the liver in pure cases of arsenical poisoning, and I cannot doubt but that arsenic will set up an interstitial hepatitis.

8. *Urine.*—In a considerable number of cases there has been a trace of albumin in the urine, but quite possibly this has been secondary to the cardiac failure. In many cases this disappears later on, so that I have no evidence to prove that there has been renal cirrhosis. We have not found any sugar in the urine. But a more interesting and important fact is the presence of arsenic in the urine of those patients who had been drinking quite recently. Professor Dixon Mann, on November 26th, obtained the arsenical reactions quite easily from only six ounces of urine passed by a woman who had been recently drinking, and its presence in the urine has also been detected by Dr. J. H. Abram and Dr. Nathan Raw[2] and others. There is no doubt, also, that the arsenic is excreted by

[1] 'Brit. Med. Journ.,' December 22nd, 1900, p. 1815.

[2] Ibid., December 8th, p. 1683.

the milk, as I was informed by a mother who was affected that her suckling child vomited after each meal (which had never been the case with any of her previous children); Dr. Taylor, of Salford,[1] reports also a clear case of the suckling infant being affected.

9. *Temperature.*—In the early stages in several cases the temperature has been raised, varying from 101° or 102° F. in the morning, to 102° to 103° in the evening, the other signs of early arsenical poisoning being fairly acute. In some cases this pyrexia has disappeared after a week or ten days in bed; in other cases it has lasted two or three weeks, and in a few has continued until death. Thus in the early stages in previous epidemics there has been some excuse for the cases having been diagnosed as influenza or even as typhoid fever.

Summary of symptoms and order of sequence.—From the above account it is clear that arsenic is almost certainly a cumulative poison, although some authors say that it is not so. Moveover, it is a poison which affects both the skin and the respiratory and digestive mucous membranes, the nerve-trunks, both sensory and motor, the muscles, including the heart-muscle, and the liver. As regards the sequence of the symptoms, Brouardel[2] has clearly laid them down, and I can confirm his statements; the sequence is—(1) digestive symptoms; (2) laryngeal catarrh, bronchitis, and acute skin symptoms; (3) disturbances of sensibility; and (4) motor paralysis (and pigmentation and keratosis). Widal, in the 'Hyères Epidemic,' gives the following actual dates in one of his cases:—February 8th, gastric disturbance and diarrhœa; March 4th, acute cutaneous eruptions, spasmodic cough, running of the eyes and nose; March 31st, sensory disturbances in the limbs; then, some days later, paresis of the upper and lower limbs. Health was only restored after one year.

The course of the disease is a slow one, the gastric

[1] 'Medical Press and Circular,' December 5th, 1900, p. 585.

[2] 'Annales d'Hygiène,' 1889, p. 479.

coryzal and laryngo-bronchial symptoms pass off first, then the acute skin lesions, which pass on to the chronic skin lesions, which I think will be found to last many months. The erythromelalgia and sensory symptoms are still almost as marked as ever in patients whom we have had under observation for four or five months, and judging from analogy of so-called alcoholic paralysis, the motor disturbances will last for from eighteen months to two years before they entirely disappear.

Mode of death.—In most of the cases this seems to be from cardiac failure, either quite suddenly or gradually. Some patients have died from paralysis of the diaphragm, with secondary broncho-pneumonia, and in one case at least phthisis contributed to the fatal issue.

Classification of cases.—The cases may be roughly divided into groups:—(1) Those with all symptoms fairly well marked; (2) those with skin lesions principally; (3) those with cardiac and hepatic lesions principally; and (4) those with paralytic lesions principally.

A careful examination into the history and present state of any case will, however, reveal some concurrent symptoms quite characteristic of arsenical poisoning. Thus, in a fair-complexioned woman who had no apparent symptoms but paralysis, which could not be diagnosed from so-called alcoholic paralysis, there was in addition keratosis of the soles of the feet.

Diagnosis.—Once the possibility of arsenic poisoning is recognised, there is no difficulty whatever in diagnosis. There is no other disease which will produce the same grouping of symptoms. In the early stages it is possible to mistake the condition for measles or scarlet fever, and in the later for Addison's disease, and in some cases it will be difficult in the present state of our knowledge to say that certain cases cannot be entirely explained by chronic alcoholism. Only a thorough consideration of the history, and full examination of the patient, will prevent mistakes being made. In beri-beri there are said to be but few skin lesions.

Treatment.—I shall say little on this point, for having entirely stopped the intake of the poison, the treatment becomes merely a matter of dealing with symptoms. One point, however, is of great importance; on account of the alarming heart symptoms from muscle failure no depressing drugs should be given. We must thus avoid potassium iodide, sodium salicylate, antipyrin, exalgin, phenacetin, etc. Small doses of digitalis, with some other diuretic, tonic doses of strychnine, gastric sedatives, carbonate of ammonia and senega will probably be required. For the pains we must have recourse to small doses of morphia. The burning sensation in the hands and feet is much relieved by spirit lotion. The other skin lesions must be dealt with *secundum artem*, but this is a subject which I would rather leave to the dermatologists. The treatment of the neuritis does not differ from that which is already well known.

Previous epidemics.—Space will not allow me to do more than mention some previous epidemics of arsenic poisoning. Graves[1] mentions that he had witnessed part of the curious "épidémie de Paris," which occurred in 1828, in which there were peripheral neuritis, acrodynia, and many other of the symptoms which I have above described. There can be little doubt that this was an epidemic of arsenic poisoning. I have been unable to find Chomel's original paper, but Barthélemy[2] says, also, that it appears to have been due to arsenic, and that in four or five months it caused the deaths of 40,000 persons on the western bank of the Seine, near Paris. Brouardel and Pouchet[3] call attention to an epidemic affecting nearly 500 persons at Hyères in 1888, and reported by Widal, in which white arsenic had by mistake been put into wine instead of gypsum; also an epidemic at Havre in 1888, in which fifteen persons were affected from arsenic

[1] "Clinical Lecture,' 'New Sydenham Society's Transactions,' vol. i, 1881, p. 578.

[2] Nielson's article in 'New Sydenham Society's Transactions,' vol. clxx, p. 237.

[3] 'Annales d'Hygiène,' 1889, vol. xxii.

put intentionally into food. Brouardel also alludes in passing to an epidemic which he had investigated from arsenic in bread,[1] and I have seen a statement made, but cannot confirm it, that in 1884, in the Départemente du Midi (France) some wine sold was found to contain a considerable quantity of arsenic, which was derived from the sulphuric acid with which the old wine barrels had been repeatedly washed, whereas the same wine which had been stored in new barrels was quite free from the poison.

Pathological anatomy.—This subject I do not intend to allude to, as it is being investigated by others. In the few cases in which I have been present at the post-mortem examinations, the only prominent signs were the interstitial hepatitis and the dilated flabby heart.

Personal statistics.—During the three months—October, November, and December, 1900—I had charge at the Manchester Workhouse Infirmary of 343 patients suffering from arsenical poisoning, 192 being men and 151 women. During November and December, at the Manchester Royal Infirmary (out-patient department), I treated 157 patients similarly affected, 99 being men and 58 women. This gives a total of 500 cases, 291 being men and 209 women. This preponderance of men over women is contrary to what I supposed at first was the case, but the symptoms were on the whole more pronounced in women. The deaths were thirteen, five of men and eight of women. The ages varied from twenty-six years to seventy years, and either beer or porter was invariably taken as a beverage alone or together with spirits. The amount taken has varied from as small a quantity as two pints (possibly only one and a half pints) to sixteen pints a day. The herpes was more common in men, for out of a total of twenty-one cases seen in three months, sixteen were in men. The heart symptoms with anasarca, and the liver enlargement and cirrhosis with ascites, were also more common in men. But the gastro-intestinal, the

[1] At St. Denis, where 250 were affected.

coryzal, and the sensory and motor disturbances were more common in women, and as a rule were shown in a much more marked degree. In eighty cases in which specially careful notes were taken, seven women out of thirty-seven had marked loss of memory of time and place, but only one man out of forty-three was thus affected. Also of these thirty-seven women twenty-seven were suffering from loss of power, ten of them to such a degree that movement of the much atrophied limbs was practically impossible. Of the forty-three men seventeen had loss of power, the loss being of a total character (in the limbs) in six cases. In all the cases of paralysis the legs were more affected than were the arms.

DISCUSSION.

Sir WILLIAM GOWERS (who could not be present, wrote as follows).—I regret that another engagement prevents my presence to-night. In connection with the subject of Dr. Reynolds' paper, it is curious to note the immunity from arsenical neuritis among those who take bromide regularly for epilepsy, and are obliged to take arsenic with it as the only means of preventing bromide rash. It is usually necessary to give at least 10 minims of Liq. arsenicalis to 60 grains of bromide to prevent acne, and many patients need 15 minims. Ten minims is equal to ·1 grain of arsenious acid. Out of a very large number of cases of epilepsy who have taken arsenic thus for years I only remember one case of arsenical neuritis. This is the more remarkable because the characteristic pigmentation is not at all uncommon, and is often intense. It sometimes causes much concern until its nature is explained, and I have often had to put before the patient the alternative choice—the bromide rash or the darkening of the skin. The latter has always been chosen without hesitation. The smallest quantity which I have known give rise to pronounced pigmentation was equivalent to about 100 grains of arsenious acid, taken during two years, of course in the form of Liq. arsenicalis. This freedom from neuritis strongly suggests the co-operation of alcohol in its production in beer drinkers. Two cases of arsenical neuritis which I have seen deserve mention. In one, which was most severe and characteristic, the arsenic had probably been absorbed chiefly by the lungs. The patient was a lady who had amused herself for years in working on æsthetic muslins, and had even slept on them at night. They were found on analysis to contain a large quantity of arsenic. The other was a man who presented symptoms closely resembling locomotor ataxy. I could not examine him thoroughly when I saw him first, and prescribed some arsenic. A month later I saw him again, and stripped him to test sensation. To my surprise and consternation his trunk was covered with characteristic arsenical pigmentation. On inquiry, I found he had been taking for at least a year a tonic pill of nux vomica and arsenic. I could not ascertain the exact amount. Under different treatment he entirely recovered; but for a long time his progress was slow.

DR. BUZZARD.—I have listened to the paper which has just been read with great interest. We must all feel that it furnishes a very remarkable addition to our knowledge concerning arsenical poisoning. There are three things I should like to

say at once with regard to it: (1) I have no doubt that the cases described belong to the group of what are called multiple peripheral neuritis. (2) I have no doubt that these cases are due, at any rate in considerable part, to the effects of arsenic, though I agree with Sir William Gowers that the influence of alchohol also cannot be excluded. (3) We cannot fail to appreciate the interesting and clever deduction that Dr. Reynolds made in tracing this epidemic to its source.

There is one point about which I feel a little doubtful whether I understood the author correctly. It appeared to me that he was greatly inclined to think that what we call alcoholic neuritis is really a form of arsenical poisoning. If this be so, and I have not mistaken him, I am prepared to join issue with him at once. I remember that in the first case of alcoholic paralysis that especially attracted my attention thirty years ago, which was that of a lady suffering from what would now be recognised as a typical attack of alcoholic neuritis, the disease was distinctly due to drinking brandy, and nothing else. My experience, indeed, has been that it is due especially to spirit drinking, In the early days of my observation of the disease its occurrence struck me as notably frequent among females of good social position, and it was always spirit that they drank—brandy in those days, just as it has been whisky more recently. The lady who drinks, drinks spirit of some kind, and the stronger wines—not beer. For some time indeed I thought it was exclusively among spirit drinkers that these cases of neuritis occurred, and it was only as time went on that I began to find them also in beer drinkers. The well-known Dr. Lettsom in a pamphlet published by him in 1789, entitled "A History of some of the Effects of Hard Drinking," referred exclusively to the drinking of spirits. He gave a singularly graphic picture of the condition now recognised as alcoholic paralysis, and he recognised as the cause of the disease excess in brandy and gin. He makes no reference to beer as a cause. But even supposing that beer was also taken by the inebriates described, we may be pretty sure that the manufacture of beer in those days did not include the use of the glucoses and inverts which the refinements of modern chemistry have placed in the hands of the brewer. So, also, Dr. James Jackson, of Boston, who gave an admirable account of alcoholic neuritis about thirty years later, said that it chiefly occurred among females, and was due to "ardent spirits."

The intense pain upon pressing the muscles, to which Dr. Reynolds draws special attention, is well known to be not at all peculiar to arsenical cases. It occurs in a very large majority of alcoholic cases. The keratoses I am not so familiar with, but I have seen considerable disturbance

of nutrition in the soles of the feet occasionally, though not very frequently, in alcoholic cases. I should like to ask the author some questions. Has he any idea of the proportion of cases which occurred in people who were really not excessive in their consumption of beer—who would take, for instance only two or three glasses a day? and secondly, whether in women of a suitable age he found that amenorrhœa was present, such as I have drawn attention to as occurring so generally in alcoholic cases? The comparative absence of mental symptoms appears to lend confirmation to the view that the cases were largely due to arsenic rather than to alcohol, but in some considerable number of his cases, where the quantity of beer drunk was very large, there must doubtless have been a mixture of both causes of neuritis.

Sir William Gowers has already referred to a point which I had intended to discuss, viz. that having had the opportunity of treating large numbers of epileptics he has seen many of them take considerable quantities of arsenic daily, along with bromide, for months or years, without displaying a symptom of arsenical neuritis. My experience quite confirms his in this respect. In contrast with this immunity let me refer to a report of analyses made by Mr. Kirkby of sixteen specimens of beer in connection with the epidemic, which showed the presence of arsenic in quantities varying from 0·01 gr. in one to 0·28 gr. per gallon in that which was most drugged. The average quantity contained would be about gr. $\frac{1}{9}$ per gallon, and a person consuming four glasses of such beer would take in the course of the day less than the equivalent of three minims of Fowler's solution, a quantity less by half than that which is taken for months together with impunity by many epileptics.

As a contribution to the question of toxic doses of arsenic let me mention a case which came under my observation some years ago. A male patient, aged 55, who took no alcohol, consulted me on account of symptoms which had commenced some months previously whilst taking arsenic for an hereditary chorea. Beginning with a dose of 5 minims of Fowler's solution three times a day, he had increased this by a minim in each dose every two or three days. At a dose of 13 minims he began to be nauseated, and omitted the drug for a few days, resuming it later in smaller doses, but taking on one occasion as much as 17 minims three times in the day. The administration of the drug (in less dose than this, however) was continued altogether for about fifty days, with occasional interruptions. It then ceased and was never resumed, so that when seen by me he had taken no arsenic for about eight months. He reported that towards the close of the administration of the arsenic his hands—especially the palms,—and the foot soles—especially the under surface of

the toes,—had become red and tender to the touch. There had been no darting pains to speak of, but a "prickly, pins-and-needles" sensation. Cutaneous sensibility had been much impaired, and the skin of the hands had peeled. The knee-jerks had been lost. At first, after ceasing to take the arsenic, he had improved a good deal, but recently had not advanced. During the worst of his illness his feet, he said, used to feel like clogs —so heavy that he could scarcely walk, and this feeling still—eight months later—remained, though not to the same extent. His knee-jerks, when I saw him, required reinforcement. Touches on the fingers still gave rise to "prickly feelings." He was still clumsy with his fingers, but had regained the power—which he had lost—of writing. There was still impaired cutaneous sensibility in the fingers and feet. He appeared to be gradually but very slowly recovering.

I calculate—though this is only an approximate estimate—that the whole quantity of arsenious acid taken may possibly have approached 13 grains (probably less), but this was concentrated into a period of about fifty days. The symptoms of neuritis were marked and severe, and eight months after the use of the arsenic had been discontinued they were still evident. This contrasts with our experience of epileptic patients who will take 20 or more grains in a twelvemonth without displaying any toxic symptoms. On the other hand, in the cases described by Dr. Reynolds, it would appear as though the administration of doses far below those commonly employed therapeutically had occasioned lesions more severe than those which occurred in the case I have mentioned. This curious anomaly stands in need of explanation.

Adjourned Discussion, February 12th, 1901.

Dr. Ormerod said:—It is my duty, having moved the adjournment of this debate, to reopen it to-night. But I only do this formally, for seeing that we have here many eminent gentlemen from the North who have been actual witnesses of this outbreak, and that, owing to the sad circumstances which prevented our debate a fortnight ago, they are here for the second time to-night, I prefer at once to make way for them.

Dr. Dixon Mann (Manchester).—You have had the clinical aspect of this outbreak well put before you by Dr. Reynolds and others, and I do not purpose going over the same ground. I will, however, say a word or two with regard to an unusual type of arsenical poisoning, of which I have seen a few cases during this outbreak. This type is peculiar, because it may occur without any of the ordinary symptoms associated with

chronic arsenical poisoning, *i. e.* without neuritis, and without any skin manifestations. In this form, of which there is more than one variety, you have a temperature varying from one to three degrees above normal; you have possibly sweating, which may be excessive, or may be hardly noticeable; you have a mental condition in which the patient is apathetic and even somnolent; if roused there is a little tendency to ramble. In two cases this mental condition was replaced by a state of mental irritability suggestive of cortical irritation. The chief indication is a singularly weak action of the heart, with dilatation and a tendency to œdema or to hyperæmia of the lungs. The patient makes no complaint; there is no pain, but he simply lies in this condition, which continues from one to several weeks. If recovery takes place it is very gradual; if the patient dies, death usually occurs rather abruptly from heart failure, which has been menacing all along. This form has been mistaken more than once for enteric fever, though there are no bowel symptoms, no enlargement of the spleen, in fact, nothing characteristic of enterica. In another peculiar form of chronic arsenical poisoning you have, or may have, absence of the usual signs of neuritis; there is no temperature, but from the first there is a condition approaching collapse, associated with diarrhœa and sometimes vomiting, very weak action of the heart, and throughout a tendency to heart failure. Of course this closely resembles the ordinary subacute form of arsenical poisoning; but it presented this peculiarity, that the symptoms did not come in one case until four and in another until seven days after the patient had ceased drinking arsenicated beer, so that it cannot be regarded as of the ordinary subacute type.

I will now pass on to the chemical side of the question. With regard to the elimination of arsenic, we have always looked upon it as a non-cumulative poison. Of course the term is relative, but we have always understood that arsenic does not remain locked up in the tissues. Now, taking the channels of elimination, we may divide them into primary and secondary, the primary being the kidneys and bowels. Years ago I showed that it was very easy to detect arsenic in the urine within half an hour of the administration of five drops of Fowler's solution; and further, from the same dose, arsenic may be detected in the first motion subsequently passed; so that the elimination commences very promptly, and under ordinary circumstances it is continuous. In acute arsenical poisoning I shall not be very far off the mark if I say that arsenic has not been found in the urine longer than from eight to ten days, that is to say, after a single dose. In chronic poisoning we have a different state of things, and frankly I was not prepared for what I found in the course of these investigations. It would appear, when repeated small

doses of arsenic are taken over a prolonged period, that the elimination rate is not able to keep pace with the rate of ingestion; there is consequently accumulation of the poison, which is backed up, rather than locked up, in the tissues. Now, arsenic does not combine with albumen in the same way that many of the heavy metals do. That it does not intimately combine with the living tissues is evinced by the fact that after large doses it is possible to obtain evidence of its presence in the urine by simply acidulating with hydrochloric acid and then passing sulphuretted hydrogen through it. This cannot be done with the ordinary heavy metals. Moreover, post mortem, a small portion of an organ, such as the liver, after a large dose of arsenic has been absorbed, readily gives evidence of the presence of the poison by means of Reinsch's test, without any preliminary preparation, showing that the arsenic is but loosely combined with the organic matter. Notwithstanding this, arsenic, when given repeatedly in small doses, does accumulate in the system, this possibly due to defective elimination. I have obtained arsenic from the urine as late as the twenty-sixth and thirty-first day after the patient had ceased taking the arsenicated beer. To put the matter beyond doubt, I may mention that I only cite hospital cases under my own care in the wards. The results of analyses of the viscera show that time is not the only factor in the elimination of arsenic from the system. I made seven investigations on behalf of the coroners of Manchester and of Salford, all the seven being women. One of these cases was in the hospital at Crumpsall for twenty-three days, and I found no arsenic in the viscera. In another, which was in hospital for fifty-two days, I found a small amount of arsenic in the liver, spleen, and kidney. Turning to the cases which did not die in hospital, I do not rely so much on the statements as to the alleged periods of abstention from beer before death. In one patient who had taken no beer for six days there was a small amount of arsenic in the liver, spleen, and kidneys. In another, described as a moderate drinker, who had had no beer for three weeks, I found an eightieth of a grain in the liver, and a perceptible amount in the kidney, spleen, and a trace in the stomach. In another, also without beer for three weeks, I found the equivalent of a thirtieth of grain in the liver, as well as a perceptible amount in the kidney and spleen, but not in the small portion of brain which I received.

Coming back to the question of elimination, the chief secondary channels are the skin and its appendages. Although I knew, of course, that arsenic was found in the skin in cases of chronic poisoning, I was not at all prepared for the large amount that is present. The keratosis that occurs offers very ample opportunity for making observations of this kind, and I have obtained a

number of specimens from different subjects, and found that in the majority of these cases very large proportions of arsenic were present. In one case I got eight tenths of a milligramme of arsenic from ten grammes of the horny, epithelial scales. In another, from three grains of horny scales, I obtained large crystals of arsenious acid. The large amount of arsenic so eliminated by the human skin is rather suggestive; and I could not help thinking that it might have something to do with the well-known efficacy of arsenic in diseases of the skin, many of which are microbic; the amount of arsenic present in the skin, after prolonged arsenical treatment, being sufficient to inhibit the multiplication of micro-organisms. In hay fever, also, the quantity of arsenic eliminated by the mucous membrane after medicinal doses may act in the same way. The arsenic in the horny scales is evidently only partially combined, some of it being soluble. By boiling three grains of the scales in distilled water for five minutes, and filtering, I obtained crystals of arsenious acid from the filtrate. Then, again, from a tenth of a gramme (gr. 1½) of nail cuttings, I got ample-sized crystals. In hair, too, a considerable amount was found. All this, of course, was known before, but arsenic was spoken of as a thing that might be found, and to insure success former investigators employed large quantities of keratin tissues, whereas small quantities will suffice. I also found that a considerable quantity of arsenic may be absorbed and eliminated without producing any obvious symptoms.

The presence of arsenic in the skin and its appendages in cases of chronic arsenical poisoning, and the ease with which it may be found, constitute a valuable aid to diagnosis after the urine has ceased to yield any evidence.

The affinity of keratin tissues for arsenic seems to me to have an important bearing, inasmuch as it may be the cause of the initial stage of the neuritis and the brain symptoms. The axis-cylinder and the white substance of Schwann are covered with a sheath of neuro-keratin, and are connected with numerous oblique and transverse fibrils. Neuro-keratin also exists in the grey and white matter of the brain; the latter contains as much as 2·5 per cent. Assuming that neuro-keratin has the same affinity for arsenic that I have shown keratin itself to possess, it is not unreasonable to suppose that this may have a determinative influence, notwithstanding the fact that multiple neuritis is mostly parenchymatous.

Dr. Judson Bury (Manchester).—This epidemic of arsenical neuritis has raised some important questions. There is the question of pigmentation; many of the cases of neuritis have shown but little pigmentation, and it is not always easy to determine whether darkening of the skin under a waist band is

due to arsenic, or is merely the result of dirt and pressure. Scaliness of the feet, too, in a form somewhat resembling that due to arsenic, is not uncommon in hospital cases where arsenic can be excluded. Then there is the important general question as to the influence of alcohol in the present epidemic. The subject of alcoholic peripheral neuritis is reopened; Dr. Reynolds has, indeed, aimed a blow at its very existence; he says that for many years he has doubted whether ethylic alcohol *per se* ever causes peripheral neuritis, and that he has never seen a genuine case of neuritis in a person who has taken whisky only. Obviously, in the future we shall have to be careful to obtain accurate information regarding the exact composition of the alcoholic beverage taken by any sufferer from peripheral neuritis. In the meantime, let us briefly consider existing evidence. I am not aware that there has ever before been a real epidemic of peripheral neuritis in Manchester. On looking through the infirmary records I find that from twenty to twenty-five cases of peripheral neuritis has been a fair average number in the hospital during a year. Last year the admissions rose to sixty-two, and these occurred mainly during the last three months, so that if the same proportion had existed throughout the year, the number of admissions would have been five or six times greater than the average. Then all over the district doctors were thoroughly aroused to the fact that there was an epidemic of neuritis. There is also the fact that sulphuric acid contaminated with arsenic was first used in the spring. With this evidence before us, there can be no doubt that arsenic, in poisonous doses, was not present in the beer that was consumed before last year. This being so, what was the cause of the twenty to twenty-five cases of so-called alcoholic neuritis that were yearly coming into hospital before the epidemic, and that may occur in the future? I presume that beer, in the future, will be free from arsenic. Does Dr. Reynolds believe that we shall have no more cases of peripheral neuritis from alcoholic beverages? Furthermore, I have seen peripheral neuritis in sailors who have taken rum, in ladies who have taken only brandy, and in other persons whose sole or chief drink has been whisky. Dr. Williamson has recently recorded a well-marked case of peripheral neuritis in a man who had taken whisky and no other form of alcoholic beverage; the whisky was analysed, and found to be free from arsenic. This case alone is enough to prove that alcoholic neuritis does occur. Now, I am unable to prove that peripheral neuritis may be caused by ethylic alcohol *per se*, but I am convinced that it occurs in spirit drinkers, and I shall continue to believe in an alcoholic form of peripheral neuritis until Dr. Reynolds or some other observer proves that it is not alcohol,

but another ingredient of the alcoholic beverage which produces neuritis. Holding this over, I may pass to a brief consideration of the diagnosis of arsenical from alcoholic neuritis. In my experience, pigmentation of the skin has not been a striking feature in the present epidemic. As a rule it has to be carefully looked for. Far more important is the erythema and the scaliness of the hands and feet. Just a word as to terminology—is it correct to call the association of erythema with pain and tenderness erythromelalgia? The latter term is usually applied to a relapsing affection, in which the redness is often limited to one foot, and affects only the lines of pressure. Now, in the cases before us the erythema is persistent, it affects both feet, and frequently involves their inner as well as their outer aspects.

With regard to the brain, although the cortical cells are doubtless in some cases attacked by arsenic, a decided mental change, with defective memory and chronic delirium, is strongly in favour of poisoning by alcohol.

Coming now to the limb phenomenon, I believe that it is impossible to exaggerate the severity of the cutaneous hyperæsthesia in arsenical neuritis. So severe is it that merely stroking the palm or the sole will cause agonising pain; perhaps its most remarkable feature is its persistence. I have a patient who has been in hospital for several months; his paralysis has almost passed away, yet cutaneous hyperæsthesia of the hands and feet is most extreme. The slightest possible squeeze of a finger or a toe, or the stroking of the soles of his feet, produces the most intense pain. Now, I do not think that hyperæsthesia of the skin is ever so marked or so persistent in alcoholic neuritis. In many arsenical cases the joints of the fingers and toes are painful and swollen; this, too, I regard as a distinction from alcoholic cases. With regard to the muscular system, if we take groups of cases we find a greater tendency in arsenical than in alcoholic neuritis—(1) to a wider distribution of paralysis; I have seen the face, the diaphragm, and the lower intercostal muscles affected in different cases; (2) to more rapid atrophy of the muscles associated with fibrillary contractions of their fibres; (3) to more rapid progress of the paralysis; thus the stages of paralysis in the hands and feet succeed one another more quickly than in alcoholic neuritis; (4) to inco-ordination of movement: ataxia is rare in alcoholic cases, it is fairly common in arsenical cases. In a type case of alcoholic paralysis the extensors of the wrist and the flexors of the ankle are predominantly affected, whereas arsenic tends to pick out and attack more severely the extensors of the fingers and toes. The arsenical foot has a peculiar hollow appearance, owing to the great increase in the instep. In the arsenical hand

the fingers are curled, and often cannot be extended, owing to contraction of the flexor tendons, the little and ring fingers being the most curled and fixed. The palmar surface of the hand, especially on the inner side, presents a close resemblance to that seen in Dupuytren's contraction.

Dr. KELYNACK (Manchester).—The clinical features of the recent outbreak of arsenical poisoning in beer-drinkers have been so fully described by previous speakers, that it is unnecessary to refer to them further, except to point out that many of the points are clearly indicated in the series of drawings, photographs, and casts which I have placed on the table. The casts are of particular interest, in that they have all been taken from patients under the care of Professor Dreschfeld, through whose kindness I am enabled to show them. Fortunately we have a few casts also of "alcoholic" cases, taken as far back as 1893, and comparison of these with the casts of hands and feet from patients with arsenical peripheral neuritis from contaminated beer shows that there is practically no difference in the muscles affected, and that the consequent deformities are similar. As regards the pathology of the condition, the effects of arsenic upon the system appear to be considerably modified by concomitant conditions. Our investigations go to show that the peculiar circumstances of the introduction of the poison have led to an increase in the rate of absorption, to exceptional accumulation in the body, and to a retardation in its elimination. We are also of opinion that the alcohol or other ingredients of alcoholic beverages have in many instances greatly accentuated the effects of the poison. A consideration of such circumstances will explain many cases where patients have only consumed very moderate quantities of beer or stout and yet suffered severely. Passing to the chemical aspect of the question, one is bound to admit there has been considerable difficulty among the analysts as to the best method of detecting arsenic in beer. Difficulties have also arisen from the fact that the acids, zinc, and other materials constantly used in testing, were found oftentimes to be greatly contaminated with arsenic. Throughout my work I have had the assistance of my friend and colleague, Mr. William Kirkby, of Owens College, and I should like to refer to his apparatus, designed to apply the Gutzeit test to the detection of arsenic in foodstuffs. It is an apparatus which, I venture to think, will prove of great assistance to chemists and toxicologists, as it greatly facilitates the ready recognition of arsenic in such compounds as beer. As to the elimination of arsenic from the body, I have seen two infants where the symptoms pointed to the elimination of arsenic in the mother's milk. In one case we obtained some of the milk, but were

unable to prove the presence of arsenic therein. We have examined a number of specimens of urine, and are able to state that there has been a continuous elimination of arsenic by the kidneys during a period of six weeks after stopping the contaminated beer. We also find arsenic to be eliminated in the desquamating cuticle, and in one patient, after five weeks' residence in hospital, we still found such a quantity present that a distinct mirror could be obtained with Marsh's test. We have formed quite a collection of hair, cuticle, and nails from these arsenical cases, and hope to have some interesting results to record in a short time. The varying quantity of arsenic in the glucose and invert sugar must be remembered when endeavouring to make clear the very difficult problem of dosage. We have had large numbers of glucose and invert sugars submitted to us, and Mr. Kirkby finds that the amount of arsenic present has varied from ·03 to ·05 per cent. It also seems that all these contaminated sugars have had an acid reaction. Then, again, as to the range of substitutes. The proportion of sugar used by different brewers to displace malt has varied very greatly. In some cases there has only been five pounds to thirty-six gallons, *i. e.* 10 per cent.; others use from 30 to 40 per cent.; and one brewer was in the habit of using 50 per cent. The glucose in this instance contained ·04 per cent. of arsenic, and the beer 1·4 grains per gallon. A large number of other bodies used in connection with making beer have been examined, but in none was arsenic found in sufficient amount to account for that found in the contaminated beers. With regard to the dosage, which to medical men is a matter of great interest and importance, one finds that the arsenic present in the beers has varied within such wide limits that it is almost impossible to ascertain the exact amount taken by any patient. For instance, if a patient drank a beer which contained ·14 grain per gallon, and took half a pint of this; that would only mean taking $\frac{1}{100}$ of a grain of arsenic at a time. Many, however, have taken quite a gallon of beer daily, and that would be something like a sixth of a grain daily. Some cases, however, have been met with taking the beer from the brewer who was using 50 per cent. of the contaminated glucose, and here the dosage was equal to 1·4 grains per gallon. The whole outbreak has raised so many problems, that time and much further research will be necessary before a complete solution can be arrived at.

Sir Lauder Brunton.—I regret much that other engagements have prevented me from hearing the admirable paper by Dr. Reynolds, in which he has treated the symptoms of arsenical poisoning so very fully that I cannot add anything to them, but perhaps I may be allowed to attempt to classify them. It is to be remembered that irritant substances, especially

if applied in a concentrated form to the skin or mucous membranes, may act directly upon them and produce local irritation and inflammation. Thus mustard in the form of a sinapism may cause inflammation of the skin, or when swallowed may produce vomiting, although none of it has been absorbed into the blood. But some irritants, especially if used in a dilute form so that their local action does not interfere with their absorption, enter the blood and are carried by it to every organ and tissue in the body. They thus reach the skin and mucous membranes from the inside, and may be eliminated by them. When conveyed in this way they may produce more intense inflammation than if they were directly applied. Arsenic is an irritant which belongs to this class. When it is brought into contact with the skin by articles of clothing or by work with arsenical materials it may cause dermatitis, and when swallowed either accidentally or purposely it may produce vomiting, diarrhœa, and inflammation of the intestinal canal. But John Hunter, Sir Everard Home, and Sir Benjamin Brodie have shown that when arsenic is applied to a wound it produces more violent and more immediate inflammation of the stomach than when the poison is administered internally, and that this inflammation of the stomach precedes any appearance of inflammation in the wound ('Phil. Trans.,' 1812, pt. i, pp. 209, 210). Brodie concludes that "it may be inferred that arsenic, in whatever way it is administered, does not produce its effect even on the stomach until it is carried into the blood." This conclusion is perhaps too sweeping, and not strictly true for arsenic in large doses and in a concentrated form; but it is probably quite correct when the poison is taken in moderate or small doses and in a diluted form, as in the beer at Manchester.

The observation of Dr. Dixon Mann that symptoms of subacute poisoning have occurred one or more weeks after arsenic had ceased to be taken confirm and illustrate these experiments. In Dr. Mann's cases it would appear that in the elimination of the poison the stomach had been affected in much the same way as in Brodie's experiments. Whilst circulating in the blood arsenic is carried to every organ and tissue of the body, and affects markedly the nervous system and muscles, the mucous membranes and skin. During the process of elimination it irritates all the mucous membranes and skin and produces corresponding symptoms. By irritating the mucous membrane of the stomach it causes loss of appetite, nausea, vomiting, and epigastric pain. In the intestine it produces colicky pains and diarrhœa. By irritating the respiratory tract it gives rise to coryza, cough, hoarseness, and oppression, retro-sternal pain and bronchitis, with occasional hæmoptysis. In the eyes it causes irritation, conjunctivitis, and œdema of the eyelids. In the skin

it produces all sorts of eruptions, three of the most marked being pigmentation, herpes, and keratosis, the epidermis peeling off the palms of the hands and soles of the feet in large flakes. Keratosis is probably due to the local action of arsenic upon the skin, for Ringer and Murrell found that in frogs poisoned by it the cuticle could be readily stripped from the body, and Nunn showed that this was due to softening of the protoplasm in the epidermis, so that it became almost completely detached from the dermis. The herpetic eruptions, however, are dependent to a great extent upon the action of the drug on the nerves. Arsenic appears to cause inflammation of the sensory, motor, and trophic nerve-fibres, as well as to act upon both sensory and motor centres in the spinal cord. It is rather difficult to decide how far the nervous symptoms are of peripheral and how far they are of central origin. The sensory symptoms are probably chiefly due to peripheral irritation, and consist in tingling, numbness, pins-and-needles, with more or less pain or burning, and extraordinary sensitiveness of the feet and of the muscles, especially those of the calf. The motor weakness also appears to be chiefly due to peripheral neuritis; but if we may judge from experiments on animals the motor cells in the spinal cord are also affected, so that the peculiar ataxic gait observed in some cases may be due to a combined peripheral and central action of the arsenic. The alterations of the nails and subcutaneous œdema are probably due to a great extent to changes in the trophic nerves. The cardiac weakness is of double origin, and is caused by fatty degeneration which affects all the muscles of the body, but especially the muscle of the heart, and also by paralysis of the cardiac ganglia. The extraordinary number of cases of peripheral neuritis which have occurred in this epidemic, together with the fact that this disease has been specially observed and described by Ross and Dreschfeld in Manchester, naturally raises the question whether peripheral neuritis may not be a disease caused in most, if not in all cases, by arsenical poisoning, and whether poisoning by arsenic may not have been going on to a greater or less extent in Manchester for many years.

A good deal may be said on both sides of this question. On the one hand, it cannot be denied that peripheral neuritis may be caused by toxins, for it is found in diphtheria, where no poison except that of diphtheria has gained access to the organism, and Sidney Martin has shown that the diphtheritic toxin, apart from the bacillus, will produce neuritis in animals. It is commonly supposed that alcohol will cause the disease, but it is by no means certain that ethylic alcohol will do so, and alcoholic neuritis in spirit drinkers may possibly be due to other substances than ethylic alcohol. A remarkable observation

was communicated to me in a letter by Sir William Gairdner, who saw many cases in Manchester about sixteen years ago, although he rarely or never saw them in Glasgow, notwithstanding the large quantity of whisky which was drunk there, and which ought to have produced the disease. When I first went to Manchester to investigate the epidemic I started with the idea that symptoms of poisoning were probably due not to the arsenic in beer, but to some other impurity; but I soon found that the arsenical origin of the epidemic could be proved beyond a doubt. The present epidemic is certainly due to contamination of beer through glucose and invert sugar made by one particular firm, who had been supplied with sulphuric acid containing a very large quantity of arsenic. But the fact that arsenic has now been found both in hops and malt renders it not improbable that cases of peripheral neuritis in Manchester may for years past have been due to contamination of beer by arsenic through the hops and malt. Although it is not yet certain, it seems probable that this contamination has arisen from the use of coal or coke containing arsenic in the process of drying the malt and hops.

Another point that arises is how far these symptoms of arsenic poisoning are due to arsenic *per se*, and how much to arsenic combined or associated with other substances. The observation that some of the patients have presented symptoms of cerebral congestion or failure reminds one of the very unfortunate experience which occurred many years ago in the laboratory of Prof. Mathieson. We know that mercury of itself has no great tendency to irritate the brain, but in making experiments with mercuric ethide, where the mercury is combined with ethyl, the two assistants both suffered from poisoning, and one had mental derangement for a year and then died. Similarly it would seem that the alcohol or some other substance in the beer has tended to direct the action of the arsenic to the nervous system. The observation of Osler, referred to to-night, seems to show that arsenic can be directed to the nervous system by combination with brandy, but it seems not unlikely, from the fact that so many of the patients suffered from comparatively small doses of arsenic, that it may either have had its action specially directed to the nervous system by the alcohol or hops in the beer, or may have been actually combined with some organic substance in the beer which rendered its action more intense. In the Middle Ages it was the custom, instead of giving arsenic itself as a poison, to poison a pig with it, or to kill it and rub arsenic into it, and then to hang it up and let it drain. The droppings were said to be more poisonous than the original arsenic. It is possible, therefore, that in beer containing arsenic there is a compound more toxic than arsenic

itself. I have secured the assistance of Professor Hewitt in investigating this subject, and we hope before many months to make a report upon it. There is another question, namely, how far these symptoms are due, not to arsenic, but to another hitherto unsuspected inorganic poison, namely, selenium, present in the beer, but this will be dealt with by Dr. Tunnicliffe. We are much obliged to Dr. Reynolds for his admirable paper, and for the extreme interest attached to the paper and to the discussion which it has elicited.

Dr. LUFF.—I should like to add my meed of praise to Dr. Reynolds for his valuable and ingenious discovery. Having done this, perhaps he will permit me to say that in a certain book on Medical Jurisprudence, which shall be nameless, it is pointed out that in cases of peripheral neuritis of doubtful origin it is always advisable to test the urine for arsenic. Dr. Dixon Mann's results in respect of the elimination of arsenic are also very interesting. As he modestly says, the facts are not new, but, speaking for my own part, I may say that we previously had only a vague idea that there was a slight elimination of arsenic by the skin; but he has shown us that arsenic is excreted in very large quantities by the skin, nails, and hair. I believe that these results will eventually prove to be of very great toxicological importance. With regard to the question of the combined effects of arsenic and alcohol, I do not propose to discuss the problem raised by Sir Lauder Brunton, as to its being in combination with the ethyl group or other ethereal compounds present in the beer; but during the discussion this evening I had recalled to my mind a remarkable case of arsenical neuritis which I saw five years ago. It was the case of a man suffering from splenic anæmia, whom I was treating with arsenic in moderate doses, five or six minims of Fowler's solution three times a day, and who after a short time developed sudden and remarkable peripheral neuritis. It amazed me at the time, until I found he was a man who had been addicted to alcohol in more than moderate quantities. He had never shown signs of alcoholic neuritis, but I took it that he was perhaps on the verge of alcoholic neuritis, and that the addition of arsenic determined the event. I am rather surprised at one of the statements in the paper of Dr. Reynolds, that vomiting is a marked feature of this form of arsenical poisoning. I certainly differ from him, because, although the number of cases I saw during my visit to Manchester were, of course, small compared with the number he has seen, yet I took very careful notes of the forty cases I saw, and I found that vomiting was not a prominent symptom. Colic and vomiting had occurred in 36 per cent. of the cases only that I saw; and even when vomiting did occur it was generally in cases

where very large quantities of beer had been consumed, and I was inclined to ascribe it to the gastric catarrh caused by the consumption of those very large quantities of beer; in fact, it was to me a matter of interest that in contrast with subacute or acute arsenical poisoning, vomiting was not characteristic of this particular form of poisoning. I classified the symptoms of the forty cases, and in 91 per cent. the first signs were pains in the feet and loss of power, then tingling and pain in the calves, while pigmentation was present in 77 per cent.; so that it was a fairly constant symptom. As to whether arsenic is a cumulative poison, certainly we have never hitherto considered it to be so. I am bound to confess, however, that we must now alter our opinion, and admit that arsenic can be—I will not say locked up, but deposited in the tissues in a way not hitherto suspected. Dr. Reynolds mentioned a case where, six weeks after drinking the beer, bullæ appeared. That is to me most remarkable, and must point to the retention of arsenic in the skin for a long time, or else to its having produced certain nervous effects which were lasting.

Dr. TUNNICLIFFE.—From a consideration of the symptoms I have been led to search for other impurities than arsenic in the sulphuric acid. The rare metal selenium is known to produce in animals symptoms resembling those due to arsenic, though tolerance to its effects can never be produced. The effects of selenium on the human subject are at present unknown. In dogs, wasting, independent of digestive trouble, is a marked feature, and pigmentation also occurs. I have analysed the poisonous beer and glucose, and have proved that both contain selenium or selenious acid. This metal has never been looked for before in cases of alcoholic paralysis, and it is possible that it may play an important part, though undoubtedly in the recent epidemic arsenic has been chiefly to blame.

Dr. FREDERICK TAYLOR.—One remark in the paper attracted my attention, and I thought from the way in which it was made that it was going to have some bearing upon the other statements. This application I have not been quite able to see, still it is of importance in connection with neuritis, and I therefore refer to it. Dr. Reynolds says, "It may be at once mentioned that the only forms of peripheral neuritis associated with great muscular pressure and pain are the alcoholic, the arsenical, and that met with in beri-beri." I do not agree with that statement. I have certainly met with cases of peripheral neuritis, which appeared to be due to other causes, in which the characteristic tenderness of the calves was noticed. Of course I may have some difficulty in proving absolutely that none of these patients took alcohol in any form, or had arsenic, but there is no evidence of it that I have been able to find.

Within the last six or eight months I have had five cases of peripheral neuritis, in all of whom tenderness of the calves was present. One, it is true, was a case of poisoning by arsenic, administered for therapeutic purposes. She was a young girl, and, in reference to what has been said of the added influence of alcohol in such cases, I see no reason to suppose for a moment that in her the arsenic was associated with alcohol. Another is a case of typhoid fever in which the calves are still tender. Another was the case of a youth who had pleurisy, with some consolidation of the lung. This boy has had a very definite peripheral neuritis affecting the lower extremities, and there has been this tenderness of the calves. He has had no arsenic and no alcohol, and I attribute the neuritis to septicæmia. Another young woman, a nurse, in whom there was not the slightest suspicion of arsenic or alcohol, had a slight degree of peripheral neuritis, now rapidly improving. This is a case in which there is, so far, no evidence as to causation, and so there remains an element of doubt. But the most positive case is that of a woman, aged twenty-four, who, having had diphtheria a month previously, had a very pronounced peripheral neuritis with weakness of the extremities and of the cervical muscles, and great tenderness of the calves. Here there is not only no history of alcohol or arsenic, but she has neuritis from a recognised efficient cause, producing characteristic effects.

Dr. Sydney Ringer.—I wish to point out that any substance of the nature of a poison introduced into the body affects all the tissues, though some may suffer more than others. Take a potassium salt for example. This is a general poison and affects all the tissues, probably in an equal degree. If you poison a frog with it, he first loses voluntary movement, and next reflex action, while the nerves still conduct impressions; but ultimately the nerves follow, and then the muscles. Arsenic is also a general poison, and as with potash salts, the brain, cord, nerves, and muscles are paralysed; but its action is more specialised than is the case with potash salts, as is shown by its action on mucous membranes and on the skin, and I do not think sufficient attention has been drawn to its general action, attention having been concentrated on its effects on the nerves. It also acts on the muscles, and the heart muscle is early involved. Some of the muscular wasting is no doubt due to the direct effect of arsenic on the muscle itself.

Sir Dyce Duckworth.—In reviewing the interesting discussion which has taken place this evening, I have been impressed by the thought that my experience of the use of arsenic as a drug has furnished me with so little knowledge of the noxious

effects of this agent. I have employed it in all quantities up to half a drachm of Fowler's solution in the day, and have but rarely seen any important toxic effects. It is therefore a noteworthy fact, if fact it be, that the continued use of very small quantities should induce the grave results of which we have heard. We supposed we knew all the ordinary effects of the drug long before the fact of arsenical pigmentation was generally recognised, and that has only been the case for some ten or fifteen years. Yet no symptom is more common than this. I have now two children under my care, one fair and one dark, who are gradually developing pigmentation under courses of arsenic. One's thoughts go back to the Styrian arsenic-eaters, and to the practice of veterinary surgeons respecting the employment of the drug as a nutrient tonic especially determined to the skin; and the important contributions of Dr. Dixon Mann to the debate to-night indicate how certainly arsenic finds its way to the cutaneous system, and may remain there. My own belief in regard to the class of cases before us is, that the toxic effects are not solely attributable to the arsenical contamination, but are probably due to the combined effects of alcohol and possibly of some other agent in beer, both together acting differently from either by itself. We have an analogy in lead poisoning, where we find the noxious effects of this impregnation intensified by alcoholic abuse. Lastly, I would venture to hope that amongst the good results of this outbreak may be the brewing of a purer beer, and a more moderate consumption of it by the community.

Dr. NATHAN RAW (Liverpool).—The recent epidemic of arsenical poisoning in Liverpool does not seem to have been so extensive as in Manchester, although some of the cases have been of a severe type. During the last three years, out of 12,623 patients admitted into Mill Road Infirmary under my care, there have been 226 cases of alcoholic neuritis, of which number 147 have presented symptoms which might be attributed to arsenic. Of these 226 cases of alcoholic neuritis 51 died, the apparent cause of death being general asthenia, with cardiac failure in most of the cases. As bearing on the question as to when the arsenical contamination of beer commenced, the infirmary statistics are of great value, and recent disclosures at the inquest in Manchester have proved that my suggestion that the poisoning commenced in May last is probably correct. During the year 1898, 26 cases of alcoholic neuritis were admitted; in 1899, 34 cases; and in 1900, 143 cases; and whereas there were only 8 cases admitted up to the end of April this year, a sudden remarkable increase commenced in May, and steadily progressed up to January last. The manufacturer of the sulphuric acid supplied to the glucose firm admitted that previous

to last March he had supplied acid free from arsenic, but that after March 1st he supplied acid containing arsenic, and hence the epidemic. With regard to the cause of alcoholic neuritis, I am convinced that, from a careful observation of a large number of cases, beer and porter are the general drinks consumed, by far the greater number being due to beer alone; but I have certainly seen cases of undoubted alcoholic neuritis where the patients have only taken brandy and whisky. With regard to this point I was particularly struck with the fact that in Scotland one very rarely saw peripheral alcoholic neuritis, and it is well known that there the popular drink is whisky. I believe, also, that the serious lesions are caused by continual drinking of moderate quantities every day for prolonged periods, rather than to sudden outburst where large quantities are taken and rapidly excreted. The great majority of cases of ordinary alcoholic neuritis occur amongst women of the poorer classes, and in Liverpool it is the custom for women to congregate in each other's houses and send for cheap beer during almost the whole of the day. By consuming it off the premises they get what is called the "long pull," which means if they ask for a gill they get nearly a pint. I mention this, because when a patient says she has taken a pint of beer a day one can safely assume double that amount. As far back as last August I commenced a thorough investigation into the cause of this great increase of neuritis, and I actually settled upon the beer as the cause; but I put it down to an increase of drinking amongst the poor, probably due to the war and extra pay received for relatives. I certainly never suspected arsenic, and it was only when I read the brilliant discovery of Dr. Reynolds that the whole thing was made plain. The symptoms and appearances have been so ably and fully described by various observers that I will not refer to them here, but I would like to refer to a few points. My cases have been divided into two great classes: (1) acute; (2) chronic. In the acute cases the patients had invariably had a heavy bout of drinking beer, and in one marked case a man had been a teetotaler for three months, and then had taken forty-two pints of beer in three days, the symptoms appearing in forty-eight hours. In several of these cases there was marked pyrexia; the temperature in three cases reached 102·4°, with great pain in the left side, simulating pleurisy—probably neuritis of intercostal nerves. The eye symptoms are different from those observed in alcoholic neuritis; there is intense itching along the edges of the eyelashes, with puffiness and œdema of the lids, not the injected bleary eye of the alcoholic. I found arsenic in the urine in five cases out of thirty-three examined, but in no case was I able to find it after ten days from admission. The pigmentation appears to be of two kinds: one that desquamates freely in

large scales and is of a dirty brownish-black colour, and a general mahogany discoloration without desquamation at all, the discoloration simply clearing up. The pigmentation appears to require several weeks to develop, as none of my admissions have developed it since December 1st. I cannot bear out Dr. Reynolds's observations that the pigmentation is confined to dark people, as I have had well-marked pigmentation in quite fair women. The sensory symptoms have certainly been much more pronounced in arsenical cases than in those alcoholic cases noted before. The motor symptoms appear to me to be indistinguishable from those observed in alcoholic neuritis, and all my arsenical cases have been symmetrical, whilst I have had cases of alcoholic neuritis in which only one limb has been attacked. In some of my severe cases of arsenical neuritis there has been paralysis of rectum and bladder, a point rarely seen in alcoholic neuritis. When one considers the enormous number of people who have been drinking this beer, which has in some cases in Liverpool contained one and a half grains of arsenic to the gallon, one is bound to think that some people are more susceptible to it than others, as only a very small proportion have been attacked. It is apparent, too, that arsenic is a cumulative poison to some extent. It would seem, also, that the action of arsenic in the system is more virulent in the presence of alcohol than when given alone. With regard to the mental symptoms, I have observed drowsiness and hebetude, with great depression and desire to sleep constantly, but nothing special in the other brain symptoms compared with those due to alcohol alone. Four cases of arsenical neuritis have died, and most of the others are rapidly improving, some of the worst cases doing well; and although I have seen paralysis of the diaphragm three times in alcoholic neuritis, so far I have not noticed it in arsenical. After a careful observation of the epidemic, I have come to the conclusion that the sensory symptoms are more pronounced in arsenical neuritis than in ordinary alcoholic neuritis, and, although very severe at first, soon pass away. The motor symptoms tend more quickly to recover under treatment than the purely alcoholic cases, and most of my cases have almost completely recovered, although a few are making no progress. One patient, after desquamating in dark brown scales, had a secondary desquamation two months afterwards. In no case have I found the slightest trace of arsenic in the scales. So far as Liverpool is concerned the epidemic is at an end, and I have not had a new case of neuritis for two weeks. It is just possible that with greater care in the manufacture of beer, alcoholic neuritis may become much less frequent. *Microscopically* the nerves show marked degeneration, but nothing distinguishable from ordinary peripheral neuritis. With regard to the amount

of arsenic concerned, it was stated in court this morning in Liverpool that over three hundred pounds in weight of white arsenic was used every week in the manufacture of beer, so that one cannot be surprised at the results. With regard to treatment after the stage of depression and cardiac weakness has passed off, I have obtained excellent results from potassium iodide, grs. v, t. d. s., with extra nourishing food, and the continuous current, with massage of the affected muscles. I am making more minute investigations into the whole epidemic, and shall hope to be able to communicate something more definite at a later period.

Dr. Reynolds.—I thank you all very much for the kind way in which you have spoken of my discovery of the arsenical origin of these cases; I am really very much ashamed of myself that it should have gone on so long before I discovered it. On looking back it seems such a very simple thing, and I can see no reason why it was not discovered two months earlier. We were very greatly misled by our attaching too much attention to the fact of alcohol. I am willing to admit that alcoholic neuritis exists, but I am not convinced thereof. It is certain that alcoholic neuritis and alcoholic heart failure is much less common in London than in Manchester, and we always tell our students to avoid mentioning alcohol as a cause of heart failure when they go up for examination. It has now been shown that it is very difficult to get alcoholic beverages without arsenic. Sulphuric acid is largely used in the manufacture of nearly all the yeast which is obtained from brewers; it is largely present in malt, into which it enters in the drying kilns. Wines are largely contaminated with arsenic, so much so that in France they are methodically examined to ascertain its absence. I would suggest that, whereas in this present epidemic we have been seeing more the general symptoms of arsenical poisoning, it is quite possible that for many years we have only been seeing the special symptoms of very minute traces of arsenic on the nervous system. It is quite possible that very minute traces of arsenic may have a specific action on the nervous system, on the skin, etc.

I very soon found that you had to insist upon a definite answer to questions put to patients. Having found that the fingers and toes began to be affected about a fortnight after drinking the arsenicated beer—and I have one attacked a fortnight after, and then there was a history of diarrhœa and vomiting,—I did not have this history when accompanied by Dr. Luff, but one was later. The question of selenium is very interesting, and it is one that should be worked out, but as yet no observations have been possible in man, so we cannot go further in the matter. As to the tenderness of the calves, I

should have stated in my paper that the excruciating tenderness of the calves was especially associated with beri-beri or arsenic. It is not a mere ordinary tenderness, it is so great that only yesterday, when I was going down my wards with a visitor, one of these women, as soon as we got near her bed, cried out that we should not come near her, so apprehensive was she of the pain caused by examination. I know that you get pain in diphtheritic paralysis, but nothing like this. In taking the history of these drinkers, I find we are too readily satisfied with a history of spirit drinking, and we are positively pleased if we can get such an admission. Now for many years I have not rested satisfied with this confession, and when I come across a case of peripheral neuritis I have made particular inquiry as to beer. In every case I have found that beer has been drunk in large quantities. People take it because they are thirsty, and they do not count it as drink. We must not, therefore, be too ready to accept as final a history of spirit drinking in these cases, but must insist on knowing whether beer has also been taken.

THE PRESIDENT.—We who have listened to the address that has just been delivered are, I am sure, ready to admit, and it may be said the profession generally recognise, that great credit is due to the author for his early detection of the cause of the outbreak of illness that has recently occurred in certain northern districts of our country. He has placed before us this evening a most lucid and interesting account detailing the symptoms observed. I propose a hearty vote of thanks to him for his paper.

A CASE OF ACUTE LEUKÆMIA

BY

ARTHUR G. PHEAR, M.D., M.R.C.P.

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A COMPREHENSIVE account of this uncommon disease was published in 1895 by Fraenkel,[1] based on ten cases which had come under his observation. In 1898 a series of five cases was recorded in the 'Medico-Chirurgical Transactions' by Bradford and Shaw.[2] The case that I wish to bring to the notice of the Society was under the care of Dr. Haig at the Metropolitan Hospital, and I am indebted to his kindness for permission to make use of the notes.

1. *Clinical history.*—Alfred B—, aged 21, a bootmaker, was admitted to the hospital on July 15th, 1899, with a history of four weeks' illness, of which the main features had been increasing weakness, headache, with swelling and tenderness of the gums. The affection of the gums was the earliest symptom to attract his attention. He sought advice at the hospital on account of an attack of diarrhœa with abdominal pain. In the pursuit of his trade he was in the habit of holding brass nails between

[1] 'Deutsche med. Wochenschrift,' 1895, pp. 639, 663, 676, 699, 712, and 749.

[2] 'Med.-Chir. Trans.,' vol. lxxxi (1898), p. 343.

his lips, and he stated that the lips were sometimes green in consequence.

On his admission it was noted that he was remarkably pale, but without wasting, and, except for slight puffiness about the ankles, without œdema. The tongue was coated; the gums were swollen and spongy, but not ulcerated. The teeth were in fair condition. Below the jaw there was some swelling due to enlarged and hard lymphatic glands; elsewhere the glands were not affected. The abdomen was slightly distended, and on deep inspiration the point of the spleen could be felt below the costal margin. There was diarrhœa and fever. No rose-spots were found, and the result of Widal's test was negative. The examination of the heart disclosed nothing abnormal beyond a soft systolic murmur at the apex, and a systolic murmur over the pulmonary area. A few *rdles* were heard posteriorly at the base of each lung. The urine was acid; its specific gravity was 1022; it contained no albumen and no sugar. The temperature was 102° on admission, and continued raised throughout the illness, ranging for the most part between 99° and 102°, with a transitory rise on one occasion to 105°.

On July 26th, eleven days after admission, there is a note to the effect that the gums were more swollen, and in parts ulcerated. The lymphatic glands in both anterior and posterior triangles of the neck were hard and large, but distinct from one another. The glands in the axillæ and groins were also hard and slightly enlarged. The spleen had increased in size, and could be felt two and a quarter inches below the margin of the ribs. I saw the patient for the first time on this date, when his aspect was remarkable by reason of the high degree of pallor, combined with the thickened protruding lips, and the swollen submaxillary and cervical lymph-glands.

On July 27th he was drowsy and very feeble, and early in the morning of the following day he died, after an illness the total duration of which was six weeks.

2. *The state of the blood.*—The examination of the

blood showed a great reduction in the number of red, and a great increase in the number of white corpuscles. Of the former there were 1,384,000 per c.mm.; of the latter 404,000 per c.mm.; the proportion of red to white corpuscles was therefore approximately three to one. Of the white corpuscles the normal forms amounted to 19 per cent., or less than one fifth of the total number, while 81 per cent., or more than four fifths, consisted of forms of which no representatives are found in healthy blood.

Dealing first with the normal forms, it should be remarked that, though they constituted so small a percentage of the whole number of white cells, as regards their absolute number they were in great excess of the normal. In each c.mm. of blood there were 77,000 white corpuscles of normal type, as compared with 10,000 per c.mm. which may be taken as a high value for healthy blood. The 77,000 were made up as follows:

(*a*) Polymorphonuclear cells 28,000 per c.mm., or four to five times the number found in health.

(*b*) Hyaline group, including lymphocytes, large hyaline cells, and intermediate forms, 48,000 per c.mm., or about ten times the normal number.

(*c*) Coarsely granular cells of normal type 1200 per c.mm., or four to five times the normal number.

No cells containing basophile granules were seen.

I would here draw attention to the importance of expressing the number of each kind of corpuscle in absolute terms per cubic millimetre of blood. The percentage number, if standing alone, is apt to be misleading; for a low percentage number may be combined with a high absolute value, as in the case of the polymorphonuclear and other cells in the present instance.

The abnormal forms, of which there were 327,000 to each c.mm. of blood, consisted almost entirely of moderately large cells, with a diameter (in fluid preparations) of 11 to 13 μ, each cell containing a single bulky nucleus, sometimes rounded, sometimes with an indentation on one side, more or less deep, giving to it the outline of a bean.

The accompanying figure (Fig. 1), illustrating the appearance of these cells, was drawn to scale with the camera lucida from a fluid preparation made with a dilute solution of methylene blue in alcohol.[1] The relative amounts of cell-protoplasm and nucleus varied considerably. The nucleus was always large, and in many of the cells it appeared to lie excentrically, being enclosed in protoplasm, of which the greatest thickness amounted roughly to about a third of the diameter of the whole cell. In other cells (about 17 per cent.) the enveloping layer of protoplasm afforded but a scanty covering for the voluminous nucleus.

In the absence of fuller knowledge as to the nature of these cells, the name "large lymphocyte," by which they are usually described, may be conveniently retained; though it should be stated that they differed from ordinary lymphocytes in other respects than that of size. With methylene blue the nucleus did not stain so deeply as in the case of the small lymphocyte; the protoplasm, on the other hand, was coloured more deeply. The protoplasm showed a further difference from that of the true lymphocyte, inasmuch as it was not absolutely clear, but had the appearance of a fine and compact granulation. Treating fixed films with Ehrlich's tri-acid stain, no "neutrophile" granulation, such as is said to be characteristic of the myelocyte, could be demonstrated. Intermediate forms, that might suggest a transition from the small lymphocyte to the large mononuclear cells, were not found.

A few cells were present in the blood of oval shape and containing two nuclei, the parts of which did not appear to be structurally connected. The nuclei of these cells stained more deeply, and the protoplasm less deeply, than that of the large lymphocytes (see Fig. 1).

The case bore a striking resemblance in its general aspect and course to those described by Bradford and

[1] *Vide* 'Med.-Chir. Trans.,' vol. lxxxii, p. 331.

Shaw. Its leading clinical features may be summarised as follows:

a. Pallor.
b. Stomatitis.
c. Enlargement of lymphatic glands, at first limited to those below the jaw, and later general.
d. Moderate enlargement of the spleen.
e. The special leukæmic blood-state.
f. Fever of moderate degree.

3. *Morbid anatomy and histology.*—At the post-mortem examination ten hours after death, it was found on opening the chest that the *thymus gland* was persistent; it was two inches in length, and of glandular texture. The *lymphatic glands* generally, superficial and deep, were enlarged, but not to a remarkable degree; the individual glands were discrete, of firm consistence, and pale on section. The *tonsils* were much enlarged. The *spleen* was large and firm; it weighed 1 lb. 5 oz., and presented on section a uniformly deep brownish-red colour. The *marrow* from the shaft of the femur was opaque, and of a pale pink colour; it was firm, not diffluent; it was nowhere red, and nowhere translucent. The marrow juice was colourless, and fluid made from the juice showed a preponderance of large uninucleated cells similar to the large lymphocytes of the blood (Fig. 2). The lymphoid follicles of the *large intestine* were swollen, to a slight extent in the upper part, to a more notable degree in the lower part, where they formed nodular elevations of the size of a split pea, the surface of which was in some cases ulcerated. The *liver* was pale and rather firm. The *lungs*, *heart*, and *kidneys* appeared healthy.

Portions of the bone-marrow, spleen, lymphatic glands, tonsils, and large intestine, were reserved for microscopical examination.

The structure of the *bone-marrow* (Fig. 3) diverged widely from the normal. In place of a tissue composed almost entirely of fat, the marrow was found rich in cells, of which the preponderating elements were large

round cells similar in every respect to the large lymphocytes of the blood. That they were not present in the marrow simply as constituents of the contained blood is indicated by the fact that, in many parts of the tissue, the large nucleated cells were several times more numerous than the red corpuscles. In the *lymphatic glands* (Fig. 4) there were large numbers of similar cells, replacing to a great extent the smaller more deeply-staining lymphocytes with which the healthy gland is crowded. There were no blood-extravasations. The enlarged *tonsil* (Fig. 5) consisted essentially of a loose connective stroma, containing numerous large cells, each with a single, bulky, and feebly staining nucleus; a smaller number of deeply staining lymphocytes were unevenly distributed among the larger cell constituents. The newly formed tissue of the swollen *intestinal follicles* (Fig. 6) was situated almost entirely in the submucosa, being bounded on one side by the muscularis mucosæ, and on the other by the circular layer of the muscular coat. It comprised a loose stroma, in the strands of which were the characteristic elongated nuclei of connective tissue. Occupying the meshwork thus formed were a few lymphocytes, and many large cells closely resembling those in the tonsils, lymphatic glands, and elsewhere. Aggregations of similar large round cells were found in the *spleen*, and here they could be compared with the large lymphocytes which, among other blood-constituents, were included in the vascular spaces. The structural resemblance between the large lymphocytes of the blood and the large cells that formed a part of the splenic tissue was a close one.

From the histological examination it is evident that in this case there had been an overgrowth of lymphoid tissue, probably as wide-spread as is its normal distribution in the body, and characterised by the formation of cells of an unusual type, different from those which preponderate in normal lymphoid tissue, and similar to the special leucocytes which during life had been found

abundantly in the blood. So far as these leucocytes are concerned the blood-condition may probably be regarded as secondary to the general lymphoid proliferation; it should, however, be noted, that in this case not only did the blood contain large numbers of abnormal cells, but the normal white corpuscles were in an excess which involved every kind, with the exception only of the group of basophile cells. In other cases of the same disease an absolute decrease in the numbers of the normal white corpuscles per c.mm. has sometimes been recorded, affecting especially the group of polymorphonuclear cells.

DISCUSSION.

Dr. Rose Bradford.—The disease is a rare one and we know very little as to its nature. We do not even know whether the term leukæmia applied to these cases is really a suitable one. Like the cases I brought before the Society some time ago with Dr. Batty Shaw they all present certain remarkable clinical features justifying its being considered a separate entity. One cannot help thinking that the disease may be more common than it is supposed to be when one realises that the cases are, so to speak, diagnosed by accident, at any rate the cases first seen, inasmuch as they present no resemblance whatever clinically to the disease ordinarily spoken of as leukæmia. The author's case illustrates this very well. One striking point is the way in which the malady simulates a stomatitis or malignant disease of the upper jaw. In a case of this kind it was only by examining the blood and discovering the excess of white cells that the diagnosis was arrived at. This fact emphasises the necessity of more frequent and more careful examination of the blood. There is a remarkable similarity in the clinical features of the different cases, and it is sometimes possible to recognise them from mere inspection of the patient. If the term leukæmia is to be used to mean an excess of white corpuscles the term acute leukæmia is no doubt applicable to these cases; nevertheless, one cannot help thinking when one sees these cases, that whether chronic leukæmia is of parasitic origin or not it seems highly probable that this disease is the result of some infection, and possibly the mouth may be the seat of infection. Although stomatitis occurs in the ordinary or chronic form of leukæmia it does not occur with the severity or frequency that it does in these acute cases. Then, again, the lymphatic glandular enlargement is moderate in amount, and the author's case resembles some of those recorded in which the glandular enlargement was, so to speak, of a simple character, there being no hæmorrhagic character or breaking down. His case also illustrates the fact that the great excess of the white corpuscles is to be explained by the presence of an anomalous form of white corpuscle which is not present in healthy blood or only in small numbers, and over and above all that, that this excess of lymphoid tissue may lead not only to an excess of these abnormal forms but to a diminution of the normal forms. His case is a little anomalous compared with certain other cases in that the spleen enlargement was considerable. In some the splenic enlargement is moderate or even insignificant. It also conforms to the ordinary group of cases in the fact that the

medulla of the bones was affected. One can therefore readily accept the case as an example of the disease at present known as acute leukæmia. It would be very desirable that in future cases of this malady we should ascertain whether the blood contains any infective agents, preferably by methods of inoculation. Probably also it would be interesting to determine whether the blood contains any parasitic protozoa, also the medulla of the bones. These points must, however, be left for future investigation.

Dr. C. REISSMANN.—Its connection with ordinary leukæmia is of interest because, according to Ehrlich, myogenic leukæmia is due to certain toxins, to chemiotaxis drawing certain granular cells into the blood. We know that the eosinophile and other cells act in this way, but leucocytes do not respond to chemiotaxis, consequently this form is quite distinct from the medullary form of anæmia. Ehrlich believes that toxins do not produce an excess of leucocytes in the blood, which, however, follows the injection of pilocarpin, etc., by increasing the flow of lymph through the glands. Its connection with Hodgkin's disease also is interesting on account of its connection with stomatitis. There is at present a case in hospital with well-marked stomatitis, and such cases are known to become lymphatic leukæmia. It has been traced to the blood, and, inoculated into rabbits, has again been found in them. I have examined the case in the Middlesex Hospital and I have found this organism, but I find similar conditions present in the blood of normal rabbits, and although one died after inoculation with this blood no change took place in the blood. It would seem, therefore, that these parasites are only granules which swell out and undergo a peculiar change. These bodies are found in the mast-cells of the rabbit, and therefore I think they are not really parasites but only mast-cell bodies. Nevertheless the fact that the malady often commences with stomatitis may point to an infective origin.

Sir THOMAS BARLOW.—As to the source of origin one naturally thinks of some acute infection coming in through the mouth. Now the cases of acute leukæmia as described by Fraenkel, Bradford, and Shaw are a very definite group, and it is desirable for clearness of interpretation that this group should be respected, but I should like to mention a case which came under my observation some years ago in some respects resembling this group, but which I regret was not more carefully recorded, especially in regard to the examination of the blood. This case is interesting in regard to the source of origin. A little boy, aged about 6, was admitted to hospital on account of his tonsils, which had an odd sloughy look, which was at first thought to be due to a form of diphtheria, but this proved not

to be so. The case went on for a time, but the patient did not really get well, and then he got very bad hæmorrhagic stomatitis, and then he got not only enlargement of the glands of the neck, but also of the spleen and many other glands of the body, in the groins, armpits, and elbows, with intense anæmia and great increase of leucocytes. There was a certain amount of fever, and to the best of my recollection the illness lasted two or three months, when he died. There was no true suppuration, but there was a certain amount of central necrosis of some of the glands. I cannot give the details of the blood examination, but the great excess of leucocytes is certain. This case is different in two or three features from the cases recorded by Bradford and Phear, yet they have certain points in common. The important point is the definite starting of the disease in an anomalous tonsillar affection, and then the stomatitis with enlargement of the glands and the blood-change. It seems to me that the element—what I may call the mouth element—in these cases of acute leukæmia is so very strikingly different from ordinary cases of leukæmia that it amounts to a distinctive feature. It may be possible to forecast that in many of these grave blood diseases, we may find an infective starting-point in the mouth or pharynx.

Mr. W. G. SPENCER.—These various groups of cases run into one another as the author has been careful to point out. He has insisted on the necessity of examining the blood, and this applies particularly to cases which come first into the hands of the surgeons. Of course, the affection is for a time at the beginning local. No doubt in time we shall make some advance in respect of the presence of organisms lying at the root of these lymphatic diseases. The only way in which we can guess at the points of entrance is by supposing that they cause enlargement of lymphatic glands; for instance, in the present case the last speaker assumed that the disease may have passed in through the mouth, and it is mentioned that the tonsils were enlarged, and possibly they may have opened the door to the infection as they do to tuberculous disease. It is also mentioned, and there are many other cases which accord with the view, that the disease may enter through the intestinal mucous membrane as in the cases which follow typhoid fever. In other cases surgeons see this general enlargement of the lymphatic glands bringing about the death of the patient commencing in the axilla or groin. These are called lymphosarcoma or malignant lymphadenoma, and later there is enlargement of the other lymphatic gland structures. Although no two cases are alike, minor changes may be discovered in the blood. In other cases the entrance has appeared to be in the naso-pharynx in what were at first called adenoid vegetations. In others the lymphatic

gland structures of the conjunctiva have become enlarged, followed by a corresponding process elsewhere. Doubtless, by-and-by, some common organism will be found to be at the root of these diseases.

Dr. PHEAR.—In my case there was, I think, no doubt that the mouth condition was the first thing to attract the patient's attention, the first indication that he had of anything unusual in his state of health. In some of the recorded cases the stomatitis was not the primary symptom, the patients having been under observation for some time previously to the appearance of stomatitis. With regard to the relation of this disease to ordinary lymphatic leukæmia, a fairly sharp line can be drawn between the two. In the first place lymphatic leukæmia of the ordinary type, although by no means common, is much more common than acute leukæmia of the type to which my case conforms. Then, again, the disease runs a more rapid course in acute leukæmia than in the ordinary form. In the authenticated cases of acute leukæmia the duration has seldom, if ever, been more than eight weeks, on an average not more than six. In the cases recorded by Bradford and Shaw the average was, I believe, about six weeks. In most of Fraenkel's cases, at any rate in those in which the diagnosis was beyond question, the duration was about the same. Among other points of difference, in the ordinary type it is the small leucocytes which are in excess, whereas in acute leukæmia the anomalous blood-cells are characteristic, differing in many important respects from small leucocytes.

DESCRIPTION OF PLATES XV AND XVI.

A Case of Acute Leukæmia (Dr. ARTHUR G. PHEAR).

FIG. 1.—Cells from a fluid preparation of blood, diluted with a 2 per cent. solution of methylene blue in 40 per cent. alcohol.

a. Large lymphocytes with bean-shaped nuclei and abundant protoplasm.

b. Large lymphocytes with rounded nuclei and scanty protoplasm.

c. Cell containing two distinct nuclei.

FIG. 2.—Hæmatoxylin and Ehrlich's tri-acid stain.

To show the close similarity of the large mononuclear cells in the marrow juice to those of the blood.

A. Blood-film.

B. Film from marrow juice.

FIGS. 3 to 6 are camera lucida drawings of sections stained first with hæmatoxylin, subsequently with Ehrlich's tri-acid stain, twice diluted, for 18—24 hours.

FIG. 3.—Bone marrow from femur.

r. b. c. = red blood-corpuscle.

n. r. b. c. = nucleated red blood-corpuscle.

l. = lymphocyte.

l. l. = cells closely resembling the large lymphocytes of the blood.

FIG. 4.—Lymphatic gland.

l. and *l. l.* as in fig. 3.

FIG. 5.—Tonsil.

l. and *l. l.* as in fig. 3.

FIG. 6.—Lymphoid follicle of large intestine.

l. l, as in fig. 3.

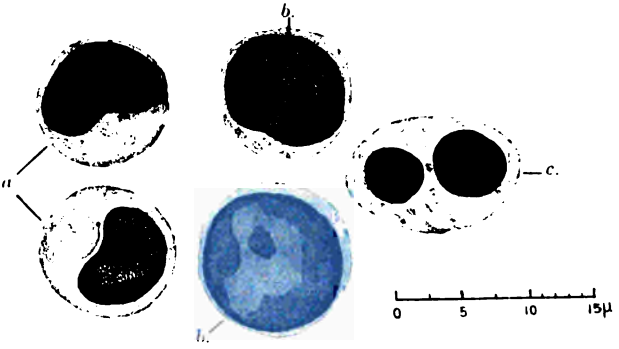

Fig. 1

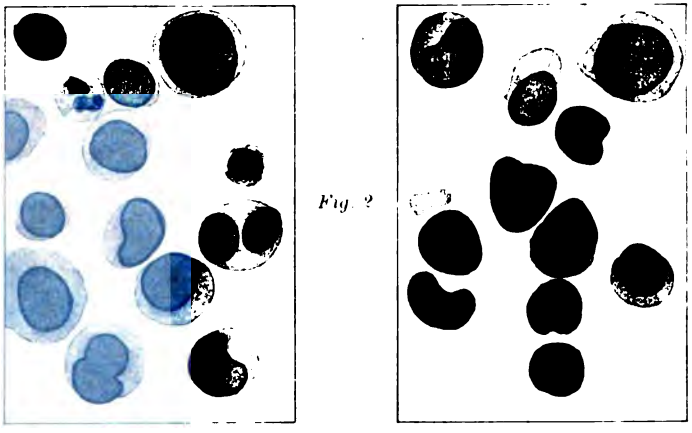

Fig. 2

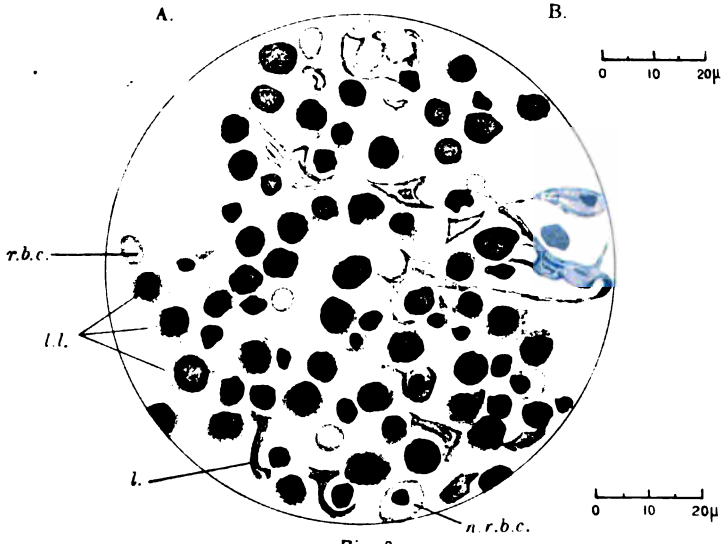

Fig. 3.

A.G.P. del. Bale & Danielsson, Ltd., Chromo-Lith.

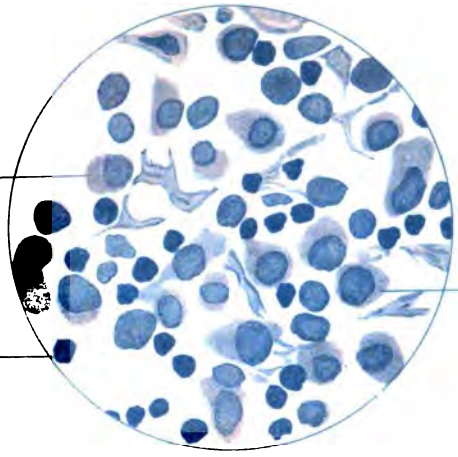

Fig. 4.

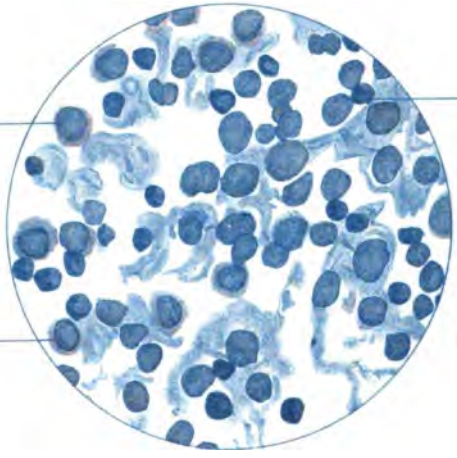

Fig. 5.

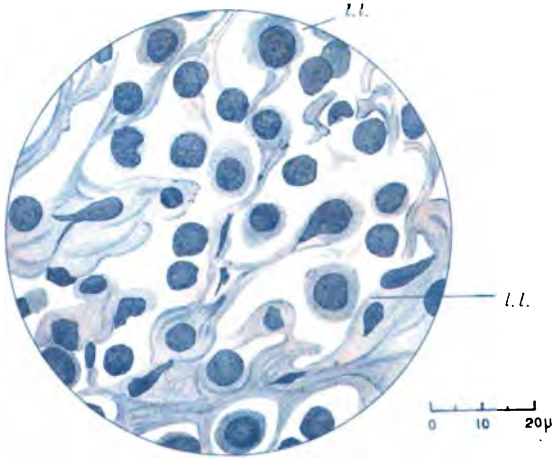

Fig. 6.

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Bale & Danielsson, Ltd., Chromo-Lith.

A PHARYNGEAL POUCH OF LARGE SIZE REMOVED BY OPERATION

BY

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The Clinical part of this case is described by Mr. Godlee, the Pathological for the most part by Mr. Bucknall.

Received 8th April—Read 14th May, 1901

THE patient whose case forms the subject of this paper came under Mr. Godlee's observation accidentally on May 18th, 1900. He had then a swelling, which looked exactly like an enlarged gland, on the left side of the neck at the level of the hyoid bone in front of the sterno-mastoid. It was, however, soft, and on percussion gave a tympanitic percussion note, and was clearly anchored to the top of the larynx, the movements of which it followed during deglutition. On squeezing it a squeaking

sound was produced, and a most uncomfortable sensation was experienced by the patient, which shot up to the ear, and which lasted for some days. The pressure caused an obvious diminution in the size of the tumour. It was clearly, therefore, a case of pharyngeal or possibly œsophageal pouch.

He was seen once more during the next few days, and in view of the serious symptoms that usually, sooner or later, are said to supervene in these cases, he was urged to allow the pouch to be removed while it was still small, but he could not at this time make up his mind to accept this advice.

He was not seen again until December 31st, 1900, when he was admitted to University College Hospital, and the following history was elicited:

The patient, who is thirty-one years old, had been in the habit of smoking to excess, and had habitually taken more alcohol than was good for him. Twelve years previously he had received a blow from a fist on the left side of the neck, which was painful, but was followed by no special symptoms at the time. Two years later he began to feel something working up and down the left side of the neck on swallowing. It was not always present, but occurred from time to time, but no fresh symptoms occurred until about three years ago.

During the last three years he had been liable to acute attacks, lasting usually about a fortnight, during which a lump developed at the left side of the neck, and swallowing became difficult and painful, until at last he could only swallow liquids. At the end of the attacks the lump disappeared, sometimes gradually, sometimes suddenly during the night. He had had about seven such attacks, and also slighter ones which he had cut short by squeezing the lump, which always caused the expectoration of a quantity of phlegm, and almost daily he had coughed up what he described as "a piece of flesh," about one inch long and curled up, which sometimes stuck in his throat, and caused him to choke and vomit.

A full feeling in the neck warned him some twenty minutes before the commencement of an attack.

The last attack began on December 21st, and resulted in a much larger and more painful swelling than had ever occurred before, and the skin for the first time became red over the swelling, though the redness was evidently not inflammatory. On admission the swelling presented the appearance shown in the photograph (Pl. XVII). It reached the middle line in front, and the posterior border of the sterno-mastoid behind, overlapping and pressing back this muscle. It reached upwards to a point just above and behind the angle of the jaw, and downwards to the clavicle, the upper border of which it just overlapped. He said that it had extended still further back a few days previously. It projected fully an inch and a half from the normal surface of the neck.

The tumour was very painful and tender, the skin was movable over it, and it was freely movable over deeper parts, except near the upper part of the larynx, to which it was fixed, and at which part it appeared to be thickened, though the rest of the swelling was evidently a very thin-walled cyst. The carotid vessels passed behind it. The percussion note all over it was tympanitic. When he held his breath and blew he could slightly inflate the tumour, which procedure produced a slight change in the percussion note.

There was no enlargement of the cervical glands, and no sign of pressure on nerves, though the voice was harsh and metallic. A larnygeal examination showed the parts to be normal, and that the cords moved freely. The temperature was normal.

Operation.—The pouch was removed on January 2nd, 1901, by a long incision over the most prominent part of the tumour. It was a delicate matter to dissect the thin skin from the surface of it, and whilst doing so the lump collapsed. It was not apparent that the wall had been pricked, but it is possible that this may have been the case. The anterior border of the sterno-mastoid with

the spinal accessory nerve entering it was drawn back, and the thin lower part of the cyst was then opened in order to make it easier to dissect it from the subjacent structures. The dissection was less difficult when the thicker upper part of the pouch was reached, and this was found to consist of two portions communicating by a rather small opening. At last the narrow pedicle was reached which passed through the thyro-hyoid membrane; but very careful probing failed to discover the actual communication with the pharynx. The superior laryngeal nerve was not seen. The thyro-hyoid was stretched over this deeper part of the cyst, which lay altogether in front of the large vessels. The tubular pedicle was then secured by catgut stitches, a fresh portion of it being divided as each stitch was passed. Finally the stump was invaginated by four stitches passed after the manner of Lembert's sutures, and the larger wound was closed except immediately over the site of the pedicle, where a small plug of gauze was placed in case the stitches should give way.

The wound, however, healed perfectly, complete asepsis was maintained; the last part of the plug was removed on January 12th, and healing was complete on January 19th.

The temperature remained normal throughout.

A careful examination of the pouch after removal was made by Mr. Bucknall. The wall of the smaller upper portion was three millimetres thick, that of the lower larger part varied from one to six millimetres.

The structure of the wall was fibrous, without any muscular elements except where some fibres of the platysma were incorporated with the outer surface. The lining was throughout glistening. That of the larger sac fell into folds like those seen in an hypertrophied bladder, but that of the smaller part was almost smooth, though showing this tendency to rugosity to a less extent.

Microscopically the outer part of the wall was made up of dense fibrous tissue with few nuclei. Within this was a layer of more nuclear connective tissue, with numerous dilated venules, and in part showing signs of recent inflammation. On this, and resting on a definite basement membrane, lay the remains of the lining epithelium, which had in most parts desquamated, and was only to be found intact in the deeper crypts (Pl. XVIII). Where perfect this consisted of about three to six layers of columnar cells with oval nuclei, the superficial layers being ciliated. The deeper layers, which alone remained over the greater part of the inner surface, were columnar or cubical; the superficial ones were long and regular, and ciliated with definite free borders united to form a plane inner surface to the sac, where they were not shed or concealed by débris. The inflammatory cells, which had in parts burst through the basement membrane, had evidently been the cause of the desquamation. Close beneath the epithelial lining lay several nodules of lymphoid tissue, and here also at one spot a group of acini were cut across, resembling in every detail of their structure a mucous salivary gland. The large cubical cells composing the lining of each acinus displayed various stages of secretive activity. A few ducts were also visible (Pl. XIX).

It is possible to obtain records of nearly two hundred cases of pharyngeal pouch and fistula. They probably all arise in connection with one or other of the visceral clefts, and the following varieties occur which depend upon the position of the obliteration of the cleft:

(1) It may remain open throughout its entire length, giving rise to the complete fistula opening into the pharynx and on the side of the neck.

(2) No external opening may be formed, and a pharyngeal pouch with a blind extremity may remain.

(3) The internal aperture may become shut off from the pharynx, leaving a blind external fistula.

(4) Both internal and external openings being closed, a "dermoid" cyst of the neck may remain.

In more than a third of all the cases the fistula was complete, and of the remainder the majority presented an external fistula, either blind or with the internal orifice so concealed that it could not be found.

In several a pharyngeal pouch was observed to burst externally, giving rise to the formation of a complete fistula; and conversely the external orifice of a fistula has been known to close, giving rise to a pharyngeal pouch, or the internal orifice once patent has become occluded, and a blind external fistula has remained.

These facts point among others to the unity of origin of the various conditions. The internal orifice, when present, has always been found in the pharynx, and not, as at one time was stated, in the larynx. This has been proved by dissection in three cases, by passing the probe in twelve, by the laryngoscope in three, and by injection from below in seventeen. It is usually small, and like the orifice of Stenson's duct situated on a small papilla, but in one case it was large enough to receive the last joint of the finger. In those cases in which its anatomical position has been accurately defined, it opened on the side wall of the pharynx close to the margin of the tonsil, and frequently in connection with the fold of the palato-pharyngeus.

The external orifice, if it exists at birth, is situated at some point along the anterior border of the sterno-mastoid; it is single, and is sometimes guarded by a subcutaneous nodule of embryonic cartilage. The most common position is just above the sterno-clavicular articulation, but it may be found at some higher point along the anterior border of the sterno-mastoid, and it has been noted opposite the cricoid, on a level with the top of the thyroid, close to the great cornu of the hyoid bone and opposite the angle of the jaw. If it results from the bursting of a dermoid cyst or pharyngeal pouch, as a rule it is still generally situated at the edge of the

sterno-mastoid, but the pouch may have reached some other position before it burst, and several external fistulous apertures may in some cases be formed.

Where a complete fistula exists some varieties in its relation to surrounding parts have been noted, but in a general way it may be said to arise from the pharynx, near the great cornu of the hyoid bone, and to run down with the carotid vessels beneath the sterno-mastoid as far as the external orifice. Pharyngeal pouches and blind external fistulæ, as a rule, follow the same course.

The lumen of the canal is usually small, and its course is tortuous, especially above, and the whole pouch or fistula may form little more than a fine cord-like band extending down the neck. But in those cases in which no external orifice exists, or in which such orifice becomes blocked or closed, there is a tendency for distension to occur, and a swelling is then formed in the side of the neck which may possess the typical features of a pharyngeal pouch; that is to say, it forms a thin-walled, resonant, globular tumour, moving with deglutition, perhaps becoming more tense on forcible expiration, and capable of reduction in size on pressure. It is very rare for food to pass into the cyst, as usually happens in cases of true œsophageal pouch; it is, however, common for mucus to be expectorated, as happened in the present case.

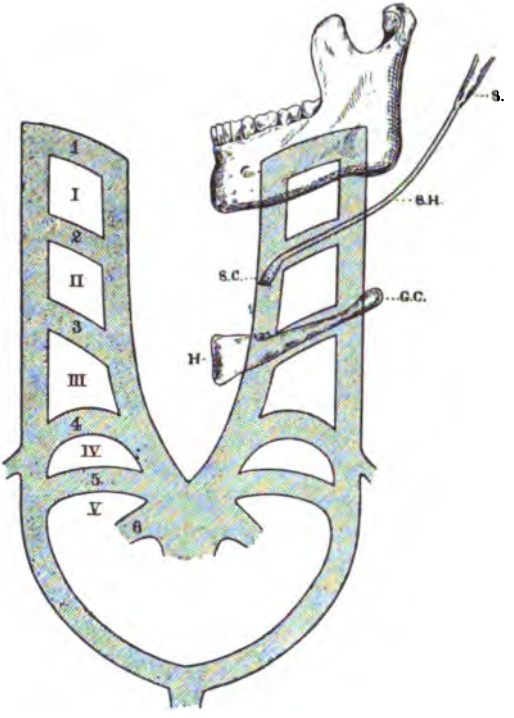
It is interesting to try to determine which of the visceral clefts is concerned in the development of such a cyst. But the problem is a difficult one, and the difficulty is increased by the uncertainty existing at the presnt time with regard to the structures that correspond to the particular clefts and arches; and it must be added that, as neither of us is a skilled embryologist, all information on these matters had to be taken at second hand.

It is generally held that in the first (or mandibular) arch the lower jaw is developed; in the second the styloid process, the stylo-hyoid ligament, and the small cornu and part of the body of the hyoid bone; in the third the great cornu of the hyoid bone.

The relation of the larynx to the visceral arches has not been determined.

As the neck of this pouch passed through the thyro-hyoid membrane, it is clear that it could not have been

FIG. 1.



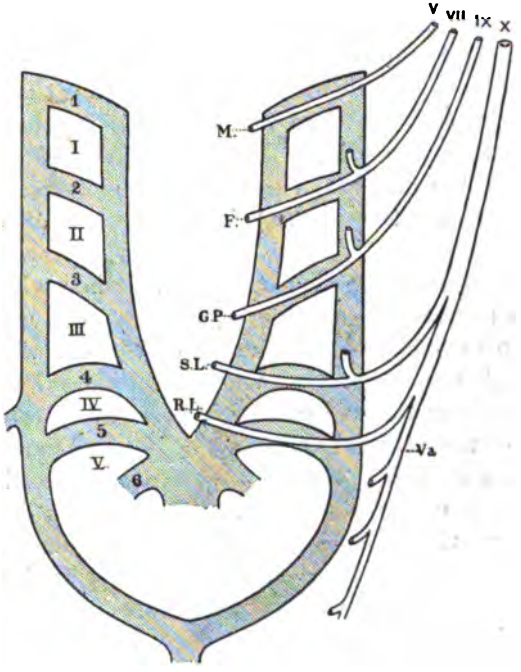
I—V. Visceral clefts.
1—6. Visceral arches.
S. Styloid process.
S.H. Stylo-hyoid ligament.
S.C. Small cornu of hyoid.
G.C. Great cornu of hyoid.
H. Body of hyoid.

connected with any cleft above the third (Fig. 1). It remains to be seen whether, supposing it was connected with the third, it bears a right relation to vessels and nerves.

The relation of nerves to the upper clefts is held to be

constant, and is shortly as follows (Fig. 2). The nerve that is associated with each cleft divides at the dorsal end, and is distributed partly to the arch above (anterior) and partly to the arch below (posterior). Thus the seventh nerve is distributed partly to the first arch and partly to

FIG. 2.



I—V. Visceral clefts.
1—6. Visceral arches.
V—X. Cranial nerves.
M. Third division of V nerve.
F. Facial nerve.
G.P. Glosso-pharyngeal nerve.
S.L. Superior laryngeal nerve.
R.L. Recurrent laryngeal nerve.
Va. Vagus nerve.

the second; the ninth (glosso-pharyngeal) partly to the second and partly to the third; and the tenth (vagus) partly to the third (external laryngeal) and partly to the fourth arch and to lower parts of the body. Unfortunately the position of the external laryngeal was not

ascertained at the time of the operation ; the main trunk of the vagus was certainly behind the neck of the pouch. It is not possible, therefore, to say whether the external laryngeal was in front of the neck, as it ought to have been if the pouch were connected with the third or some lower cleft; it is, however, almost certain that it did occupy this position.

The relation of the carotid arteries to the clefts is not yet definitely settled, and the issue is confused by the fact that the embryo of the chick has been so much employed in the study of embryology, and that the development of the carotids does not appear to be the same in birds as in mammalia. Another source of confusion arises from the fact that the vessels are displaced downwards (towards the thorax) in the course of development.

The accompanying diagrams (Fig. 3) show what, as far as we can ascertain, is considered by many good authorities to be the developmental relation of the carotids to the arches. According to this view, the external carotid is developed from the ventral aortic vessel, and thus passes in front of the visceral arches; the internal carotid from the third arch and that part of the dorsal aortic vessel which is above (anterior) to it.

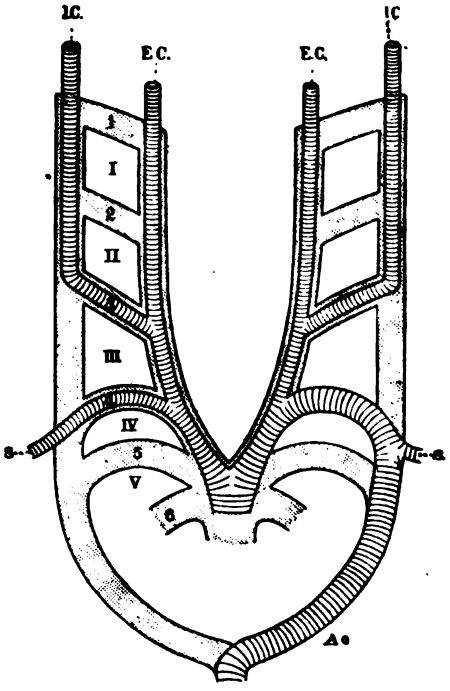
If, then, this pouch were developed from the third cleft, its neck ought to have passed behind the two carotids. But such was not the case. Both carotids were behind the neck, and only one explanation suggests itself—that the pouch was quite small at the time when the vessels were being displaced downwards (towards the chest), and that in its subsequent growth it pushed up in front of the external carotid.

If we turn to the descriptions of other observers, it is found that it is not infrequent for the neck of the pouch to pass between the external and internal carotids, and that the relation of some of them to the second cleft appears to have been clearly made out.

Thus König, Watson, Heuter, Rehn, Tricomi, and

Gussenbauer, all noted that the canal passed beneath the lower border of the digastric, and Watson and Heuter traced it between the external and internal carotid arteries to the pharynx, the seventh nerve lying above it, and the ninth nerve and the stylo-hyoid ligament below

FIG. 3.



E.C. External carotid.
I.C. Internal carotid.
I—V. Visceral clefts.
1—6. Visceral arches.
S. Subclavian.
Ao. Aorta.

it. This seems to have been the course of the canal in the very few cases that have been dissected post mortem. Some others have been traced into the same position by operation, but though a few others, like the present case, have been traced up to the thyro-hyoid membrane in an operation, the exact position of the internal opening has

not been ascertained. In Watson's case a branch of the ninth nerve innervated the walls of the pouch, and in the case recorded by Berger probing of the fistula caused cough and stopping of the pulse and other symptoms of distress thought to be due to irritation of the superior laryngeal nerve. In Cavazzani's case vomiting followed the use of the probe.

In most cases the walls were found to consist of fibrous tissue, and striped muscular fibres have been noted by some observers. The lining epithelium was either of the stratified flattened variety, or columnar and ciliated as in the present case. König noted two canals side by side, one lined with flattened and the other with columnar ciliated epithelium, and other observers have described pouches lined with flattened epithelium below and columnar and ciliated at the upper part,—that is to say, the part of the pouch nearest the pharynx.

The facts pointing to the congenital origin of pharyngeal pouches and fistulæ, and to their probable connection with the visceral clefts, may be summarised as follows:

(1) They are frequently hereditary.

(2) They are often bilateral.

(3) Though they often do not appear till early adult life, they may be present as fistulæ at birth or very early in life, and it is probable that they are often overlooked, as the symptoms they give rise to are slight and may take some time to develop.

(4) The peculiar course of the canal.

(5) The presence of a lining of ciliated epithelium, although they are derived from a portion of the pharynx normally covered with squamous epithelium.

(6) The fact that the neck of the canal or pouch often passes between the carotids in the position of the second visceral cleft.

(7) The fact that striated muscle has been found in the wall of such pouches and fistulæ, and that in one case a band of striated muscle ran from the end of the

pouch down the course usually pursued by complete fistulæ.

(8) The fact that in several cases glands having a similar structure to the normal mucous salivary glands have been found opening into the lumen of pouches and fistulæ. This may account for the discharge noted in cases like the present. One of us has met with an instance, many years ago, of a cyst, then supposed to be developed in connection with the bursa beneath the hyoid, which was, however, lateral in position, and which it was found impossible to dissect out. The patient, who was under the care of Lord Lister, was a distinguished advocate, and he was much troubled after the operation by a mucous discharge from the fistula, which occurred when he was speaking in court. The fistula, after many years, closed.

(9) The fact that around the lumen a considerable quantity of lymphoid tissue was noted by König in three cases, and also by others, while cartilage has occasionally been met with in the walls of such fistulæ.

As this pouch was obviously of the pharyngeal variety, no reference is here made to the so-called pressure pouches of the œsophagus, but it is at least possible that some of these should be placed in the same category.

Bibliography.

The following references include nearly all the recorded cases. The writings giving most information on the subject are marked with an asterisk.

* Kostanecki and von Mielicki.—Archiv für path. Anat., 1890, cxxi, pp. 55 and 247. Containing a summary of all cases up to the year 1890.

Sachs.—Jubiläum, von Theo. Kocher, Wiesbaden, 1891, p. 63.

Hektoen.—Chicago Med. Rec., 1891, ii, p. 128.

Tietze.—Zeitsch. f. Chir., Leipzig, 1891–2, xxxii, p. 421.

Tricomi.—Riforma Med., Napoli, 1891, iii, p. 541.

Cavazzani.—Ibid., 1891, iv, p. 31.

* Paci.—Sperimentale, 1891, xlv, p. 425.

* Lejars.—Progrès méd., Paris, 1892, xv, pp. 113—117.

Berger and Février.—Bull. Soc. de Chir., Paris, 1892, xviii, pp. 75—80.

* Gussenbauer.—Beitrag zur Chir., v. Billroth, 1892, pp. 250—286.

Arndt.—Berlin. klin. Wochensch., 1892, p. 532.

Shattock.—Path. Soc. Trans., Lond., 1892, xliv, p. 62.

Schlange.—Archiv f. clin. Chir., Berlin, 1893, xlvi, pp. 390—392.

* Karewski.—Archiv f. path. Anat., Berlin, 1893, cxxxiii, pp. 237—249.

Buscarlet.—Revue méd. de la Suisse, 1893, xiii, p. 1.

Sulicka.—Thèse doct., Paris, 1893–4, No. 492.

Parker.—Bristol Med.-Chir. Journ., 1893, xi, p. 1.

Hamann.—Cleveland Med. Gaz., 1893–4, ix, pp. 110—112.

* Giordano.—Riforma Med., Napoli, 1895, xi, pp. 530—544.

Kopfstein.—Wien. klin. Rundschau, 1895, ix, p. 401.

Lichtwitz.—Gaz. hebdom. d. l. Soc. d. Méd., Bordeaux, 1895, xvi, p. 471.

König.—Archiv f. klin. Chir., Berlin, 1896, li, pp. 578—618.

Kontnik.—Gaz. hebdom., Paris, 1896, xliii, pp. 1216—1218.

Binnie.—Kansas City Med. Index, 1897, xviii, pp. 49—53.

Von Hacker.—Centralbl. f. Chir., Leipzig, 1897, xxiv, pp. 1073—1076.

De Stella.—Annal. Soc. d. Méd. d. Gand, 1898, lxxviii, pp. 174—181.

* Sultan.—Deutsch. Zeit. f. Chir., Leipzig, 1898, xlviii, pp. 113—155.

Vaughan.—Brit. Med. Journ., 1899, i, p. 148.

* Nieny.—Beitrag z. klin. Chir., Tubingen, 1899, xxiii, pp. 89—108.

Pouches similar in many ways to the one forming the subject of this paper are described by Watson, Pertick, Zuckerkandl, Kirchner, Schmidt, Kostanecki, and Kopstein. The references of the first six will be found in Kostanecki's paper, mentioned above.

DISCUSSION.

Sir FELIX SEMON.—Perhaps the most important part of the paper refers to the unity of the various forms of congenital malformation met with in the front of the neck. Formerly it was held that these various forms, diverticula of the pharynx, complete or incomplete fistulæ in front of the neck, and cysts, were of different origin, and it is the great merit of Kostanecki that he, in 1890, for the first time established the unity which has been so admirably and clearly demonstrated in this paper. That is a point of great practical importance. I was astonished to hear that as many as two hundred cases are already on record. I myself have only seen two such cases, of which one belongs to the variety described in this paper, the second being a case of incomplete fistula. It was one in which there was a slight mucous discharge on the right side of the neck on a level with the larynx in front of the sterno-mastoid. It was possible to probe it up to the pharynx, where it ended blindly, but its origin was obviously close to the tonsil. I explained to the patient that a cure could only result from dissecting out the whole of the fistulous tract, and that apparently discouraged him. My second, or rather my first case, was one which I am not likely to forget, for I found myself in the position of the sorcerer's apprentice in Goethe's poem, who could not get rid of the spirits he had invoked. The patient was a young gentleman who wished to enter the army. He had a swelling on the left side of the neck which his medical attendant thought was thyroid, but on examining him it was obvious that, unless there was thyroid tissue quite separate from the main body of the gland, it could not be that, for it was situated between the hyoid bone and the lower border of the cricoid cartilage, occupying almost the position shown in Mr. Godlee's diagram, but was not nearly as large. It was egg-shaped, distinctly moveable, did not seem to have any pedicle, was not tender to the touch, and showed some indistinct fluctuation. I thought it was probably a simple cyst, and I probed it, evacuating a considerable quantity of what looked like ordinary pus, and the tumour collapsed. Within a week it filled again, and a large quantity of caseous *débris* came away. I enlarged the opening, but the tumour always immediately refilled. I need not weary you with the clinical details beyond saying that it would not close in spite of every treatment. With the finest probe I could not detect the length and direction of the canal. I had a consultation with Sir Frederick Treves, who considered

it a sebaceous cyst. By his advice I laid it open, scraped the walls, and burned it with the actual cautery. This also was unsuccessful, and ultimately it was dissected out completely by a country surgeon, who informed me that the sac ended blindly above the hyoid bone. The case, which was observed long before the publication of Kostanecki's paper, taught me the important lesson that a fluctuating tumour in front of the neck, of the exact nature of which we are uncertain, should not be probed, unless we are prepared to go the length of dissecting the whole thing out if need be. In conclusion, I should like to ask what are the serious symptoms which the authors state are likely sooner or later to supervene. Do they refer to the possibility of this complete or incomplete fistula becoming later a so-called branchiogenous carcinoma?

Mr. GODLEE.—I may mention at once that this phrase was introduced at a time when we were thinking more of œsophageal pouches, in which inflammatory troubles are common.

Mr. BUTLIN.—I have never seen a cyst of this kind, and therefore know little about them. The only thing at all resembling this which I have seen is a specimen in the museum at St. Thomas's Hospital to which the author has referred in his paper. When I examined this specimen years ago in connection with *œsophageal* pouches I could not make it out, and was much surprised to find that it was quite on one side of the neck, and ran down from a very much higher point than do œsophageal pouches. On the other hand, I have dissected out a branchial fistula, which opened near the sterno-clavicular articulation, into which a probe was passed three or four inches upwards. I dissected it without any particular difficulty, and it was by no means a serious operation. It reached right up to the posterior palatine arch, where I invaginated it into the mouth, tied the neck, and then cut it off. The wound healed by first intention, and the boy had no further trouble. That was in 1897. I wish I had taken notes of the operation myself, for the dresser only stated that the tube lay in front of the external carotid artery, and said nothing about the internal carotid artery and the nerves. Naturally, in doing an operation of this kind, one limits one's self to the removal of the trouble without searching about to discover the relations. With regard to *œsophageal* pouches and their possible relationship to these pouches, I may say from a very extensive experience of them—for I have removed not less than seven and have seen at least twelve—they never present any external tumour like this in the neck. Then, again, they are all built so exactly upon one type, open upon the same place, and are so much the same size that they seem to have no relation at all with branchial fistulæ, and I cannot help thinking

that they are a disease or a condition of an entirely different character.

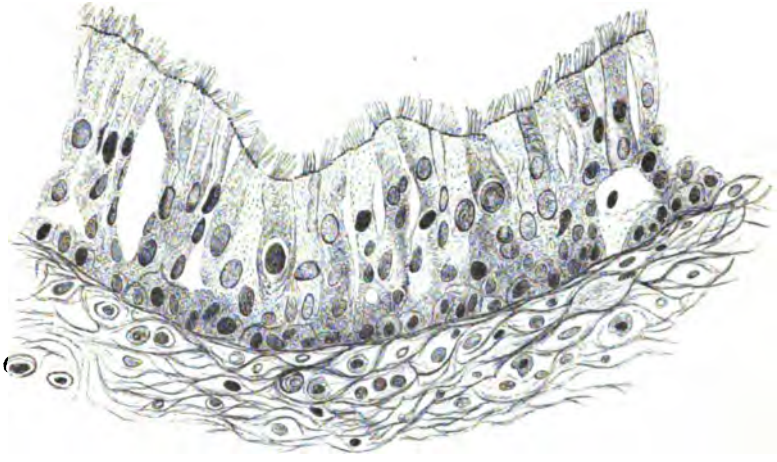
Mr. A. E. Barker.—I may mention a case which will add to the list which Sir Felix Semon has made of his cases. It presented many features in common with the one described except that it was larger and was on the other side of the neck, but there were certain points of difference, and this may add to its interest. The patient was first seen by Sir Felix Semon, but the patient was an old friend of mine, and he asked me what had best be done. I expressed the opinion that it was a dermoid cyst or pouch connected with one of the branchial clefts, and I based my conclusion on the following points:—(1) I was aware that the right auricle was badly developed; (2) down in the episternal notch I noticed a little tuft of hair, and over the centre of this a tiny depression with a little hardness around it; (3) between the two points under the lobe of the ear was a tumour about the size of the bell over the electric light. There was this feature, that the tumour varied very much in size, being sometimes inconspicuous and at others quite large. It had the soft doughy feel of an incompletely filled sac. I could not empty it, and the patient said it sometimes filled rapidly. Then, again, he felt very ill at the time, although in general good health. This suggested to me that there was an auto-intoxication going on. In view of the position of the tumour right in front of the sterno-mastoid, and of the other signs, I thought it was a dermoid, and I removed it. The relations are fresh in my memory. I made an incision from the lobe of the ear to over the episternal notch, bifurcating below to enclose the dimple. I came down upon the sac and dissected it off the carotid vessels with some difficulty, for it was closely adherent to them as the result of past inflammation. I stripped the common carotid for two or three inches and gradually got it out. It came out whole, and it narrowed further and further down to about the size of a lead pencil alone. I traced it up to just below the tonsil, and with my finger in the mouth and my other fingers grasping what I may call the pedicle, I could feel that they were close together, only the mucous membrane intervening. I put a silk ligature round it and tied it. Before doing that I made a little hole in the upper part, and the probe came right against my finger below the tonsil. I have no doubt that there was an opening there. I had sections made of the narrower part, and they showed what the author's case also shows. The point of interest is that we diagnosed it by an examination of the skin below. What cleft this actually belonged to I cannot tell. I took it to be the lowest cleft, but that may or may not be correct. Since it was taken away my friend tells me that his constitution has been quite revolu-

tionised. The incision, of course, is a very formidable one, but it healed throughout by first intention. I may mention that I have had several cases, which have been recorded in the 'Transactions of the Clinical Society' many years ago.

Mr. GODLEE.—I was rather surprised to hear Sir Felix Semon say that he had only seen one or two cases of the sort in his large experience. I was shown one of these cases quite early in the course of my experience, and since then I have seen a good number of such fistulæ opening into the neck. Mr. Butlin's remarks are always interesting, and one of the most interesting things he has said is that he has never seen a case of this kind, although he has met with so many of œsophageal pouch. When I saw the case first I must say I thought it was one of œsophageal pouch, because I have heard more about them, also because there was a history of a blow on the side of the neck, and the theory is that some of these pouches are in some way due to injury. The dangers I alluded to have been described in connection with œsophageal pouches.

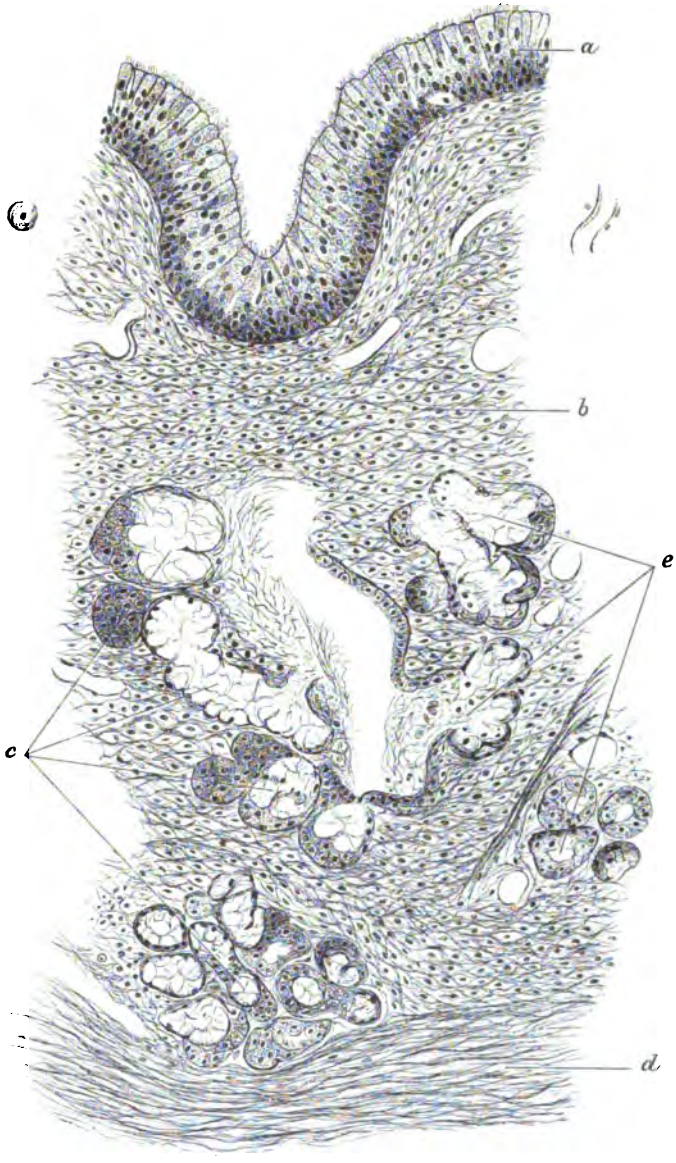
Mr. BUTLIN.—You never see an œsophageal pouch come as high up as this one did.

Bale and Danielsson, Ltd.



Lining of pouch shewing columnar ciliated epithelium.

R. B., del. *Bale and Danielsson, Ltd., Sculp.*



WALL OF POUCH shewing—
(*a*) Lining of columnar ciliated epithelium ; (*b*) Loose connective tissue ; (*d*) Dense outer layer of fibrous tisssue ; (*c* & *e*) Acini of salivary glands in the wall of the pouch.

R. B., del. *Bale and Danielsson, Ltd., Sculp.*

AN ADDRESS

ON

RECENT ADVANCES IN THE KNOWLEDGE OF MALARIA[1]

BY

PATRICK MANSON, M.D., LL.D., F.R.C.P., F.R.S.

When the subject of the malaria parasite was last before the Society, Golgi's views as to the fever or intra-corporeal cycle had already been generally accepted. There remained, however, many other forms of the parasite as seen in the blood, which were not included in Golgi's cycle, and which up to that time had not received adequate explanation, notably the crescent form, the large free spherical forms, the flagellated bodies, the free flagella, etc. These were by many, especially by the Italians and their followers, regarded as effete, moribund, "agony," or degeneration forms, on the very inadequate ground that their nature and purpose were not apparent, and because, up to that time, no nucleus had been demonstrated in such parasitic elements. The view had been

[1] Being remarks introducing Dr. L. Sambon's Report on Experiments in London and the Roman Campagna, presented at the meeting of the Royal Medical and Chirurgical Society, January 8th, 1901.

advanced by some of us that these so-called degeneration forms, because certain of them were not evolved until the blood containing them had left the human body, really belonged to the hitherto unrecognised extra-corporeal cycle of the parasite; and because, while in the human body they were still enclosed in red blood-corpuscles and therefore could not escape in virtue of their own efforts, that they must be abstracted and nursed, so to speak, by some suctorial animal, which, from geographical and epidemiological reasons, we considered to be the mosquito; further, because malaria did not occur in every place where there were mosquitoes, that the malaria parasite must be subserved by a particular kind of mosquito. The complete proof of this hypothesis was supplied by Ross both as regards bird and human malaria. Important supplementary evidence was forthcoming in MacCallum's interesting observations on the fertilisation of the female gamete in the case of halteridium, an analogous parasite of certain birds. Ross's observations have now been fully confirmed by the Italians, by Daniels, by Koch, and others. Experimental proof has also been given. Grassi, Bignami, and Bastianelli have recently succeeded in experimentally conveying, by means of mosquito bite, the malaria parasite from one human being to another, just as Ross had previously done in the case of the proteosoma-malaria parasite of the sparrow.

In consequence of these observations our knowledge of the malaria parasite is now so complete that we can indicate with a fair amount of precision its exact zoological position. Recent observation has shown that its place in Nature is alongside the coccidia, that its human phase corresponds to what was formerly known as the eimeria stage of these organisms, its mosquito phase to the coccidial stage. The diagram represents in comparison the life cycles of *Coccidium Schubergi* and of *Hæmomenas præcox*—the name applied by Ross to the parasite of tropical malaria. The escape of the sporozoit from the oocyst or zygote and, in the case of the coccidium,

its entrance into an epithelial cell, in the case of the malarial parasite its entrance into the blood-corpuscle, is practically the same as regards both parasites. The succeeding figures show the formation of the schizont; the multiplication of nuclei; the formation of merozoits; the breaking up of the ripe parasite; and, finally, the divergent development of the various merozoits or spores, some entering the epithelial cell in the case of the coccidium, or blood-corpuscle in the case of the malaria parasite and renewing the schizont cycle, others becoming converted into macrogametes, others again into microgametes. In both types of parasite we see that the formation of microgamete and macrogamete is conducted on exactly similar lines; in both we see the fecundation of the macrogamete by the entrance into it of the microgamete, the fusion of nuclei,—male and female, the encapsulation, the formation of the oocyst in the case of the coccidium and the zygote, as it has been termed, in the case of the malaria parasite. At this point, however, the method of development in the two organisms diverges—changes to a certain extent; whereas in coccidium the nucleus divides into four and four sporocysts are formed in the interior of each of which two sporozoits are subsequently developed; in the case of the malaria parasite the division of the nucleus is much more elaborate, the fragments becoming surrounded by protoplasm on the surface of which a vast number of sporozoits are ultimately formed. With this exception the development of coccidium and that of the malaria parasite correspond in every particular.

Ray Lankester has lately drawn attention to a singular circumstance, one which might be regarded from the biologist's point of view as an abnormality, in the evolution of the malaria parasite. In the foregoing description there is distinct evidence of parthenogenesis. Ray Lankester points to the characters of the microgamete and of the sporozoit as indications that it is conducted by what appears to be a male element, and not, as is usual, by a female element.

Unfortunately, from multiplication of terms much confusion has crept into the nomenclature of the various phases of the evolution of the malaria parasite. It is highly desirable that a reform in this respect should be instituted. It would be well that some agreement be arrived at on this subject.

Although we now know a great deal about the life-history of the parasite, much is still required to round off this knowledge. We would like to be able to say what are the circumstances which determine the destination of the merozoit, or spore; what it is that determines one of them to enter on the endogenous cycle and carry on the life of the parasite in man, and what it is that determines another to assume the characters of a macrogamete, and what it is that determines a third to take on the characters of a microgamete and provide for the exogenous cycle in the mosquito. We know nothing of the latent phase of the parasite further than that there must be such a phase; we know that malarial infections may remain latent in the human body for months, and even years; that an infection contracted in India, for instance, without showing any clinical evidence of its presence there, may, months subsequently, become active for the first time when the patient has returned to England where, perhaps, he may get his first attack of ague whilst walking down Regent Street.

Another important point calls for settlement. Is man the only vertebrate host of the malaria parasite, or, like many other parasites, has it a variety of hosts? Among the nematodes such a multiplicity of hosts is common: *Trichina spiralis, e. g.* can live in rats, pigs, dogs, men, and many other vertebrates; among the protozoa, *Trypanosoma Evansi, e. g.* occurs in dogs, horses, donkeys, cattle, and other beasts. Why not a similar multiplicity in the case of the malaria parasite? Indeed, there are some indications that such may be the case. Dionisi's recent discovery of several species of intra-corpuscular parasites in the bat, closely resembling those of man, is extremely

suggestive; all the more so seeing that the bat, like primitive man, is a cave-dweller, a troglodyte, and even accompanies him when in process of civilisation he takes to building himself a house.

Another singular feature about malarial infection is dimly indicated by recent observations in Africa as well as in Italy. Drs. Stevens and Christophers tell us that they have rarely found crescent bodies in the blood either of Europeans or of natives in Africa. Daniels, for British Central Africa, and Plehu, for Camaroon, bear similar testimony. Now I can vouch that the crescent body is exceedingly common in such patients when they come to England. At the present moment I have under observation at the Seamen's Hospital four malarials, Europeans, all of whom contracted their fever on the Niger, in whose blood the crescent parasite is present in great abundance. I constantly see similar cases. Are we to suppose that if these four men had remained in West Africa the crescent form of the parasite would not have developed, that it was only in consequence of their having left West Africa and come to a more temperate climate that this phase of the parasite was evolved? Drs. Christophers and Stevens tell us that the gamete form in West Africa, in the case of the tropical parasite, is almost invariably a non-crescentic parasite, being a simple pigmented disc of protoplasm, closely resembling the intra-corpuscular forms of the ordinary quartan parasite. This reluctance, so to speak, of the African parasite to form crescents in its native country apparently is not shared by the corresponding Indian parasite. Ross and others speak freely of this phase as occurring in India. Is the African parasite specifically different from the Indian, and, if so, why should it take to forming crescents when it comes to England? It is to be regretted that the recent expeditions to Africa for the study of malaria did not give more attention to this point.

We know now that the mosquito is the definitive host of the malaria parasite. So far it has been found only in

members of the genus Anopheles, of which there are at least forty-six species. Of these *A. funestios, A. costalis, A. claviger, A. pseudopictus, A. superpictus,* and *A. bifurcatus* have been incriminated; but how many more of the remaining forty odd are capable of subserving the parasite we do not know. Of the two hundred and fifty known species of Culex, *C. mimeticus, C. pipiens, C. tæniatus, C. nemorosus, C. malariæ,* and three unidentified species experimented with by Daniels in British Central Africa, have alone been tested and found inhospitable as regards malaria, but it is quite possible that some of the other Culices may be efficient hosts.

The distribution of malaria having been found to depend upon the distribution of certain species of mosquitoes, it is of importance, from a practical point of view, to ascertain on what the distribution of these mosquitoes depends. The study of this point must be approached from two directions. We must study the circumstances favourable to any species that may be investigated, and we must also study the circumstances which are unfavourable to such; more especially the latter, for it is quite possible that having ascertained the inimical conditions we may be able to reproduce them, and so have at our command means to destroy the dangerous mosquitoes. Studies in this latter line have not been instituted as yet, although they are in contemplation.

Much attention has been bestowed upon what is generally supposed to be a phase of malarial intoxication, viz. black-water fever. One German and two English expeditions have made it a subject of special investigation. So far, the practical results have been *nil,* although much useful information has been acquired bearing both on black-water fever and on malaria. It has been ascertained that the geographical range of black-water is more extensive than is generally supposed. Many theories have been advanced as to its nature and causation; for example, the old idea, first promulgated by the Italians, that it is an expression of quinine poisoning,

has been brought prominently forward by Koch. Whatever may be the *rôle* of quinine as a subsidiary cause it is certainly not *the* cause of black-water fever, for of late many instances of the disease have been recorded in individuals who have never taken quinine. It has also been stated that black-water fever is an intense form of malaria, whatever that may mean; if it means that it is a high degree of infection, that is, the result of a phenomenally abundant swarm of malaria parasites in the blood, the idea is certainly untenable, for in many cases of black-water fever the malaria parasite is absent, and in cases in which the patients have come to the post-mortem table, although some evidence of malarial infection is obtainable in nearly every case, in many instances the evidence is only that of a mild infection as regards abundance of parasites. Again, black-water fever is notoriously absent from many intensely malarial places, the Roman Campagna for example. One important test for malarial infection black-water fever does not respond to; it is not amenable to quinine. Another theory of its causation attributes it to malarial cachexia; this, too, is untenable, for black-water has been known to occur in individuals within a few weeks of their arrival in the endemic zone; in other cases there has been complete absence of the usual evidences of cachexia before the development of the black-water symptoms. One theory with a good deal in its favour is to the effect that black water is the result of a specifically distinct type of malaria parasite; another that it is the result of ordinary malarial infection, the virulence of the parasite having been increased by transmission through a particular but undetermined species of mosquito; yet another theory is that black-water fever is a disease *sui generis*, with its special but as yet undiscovered parasite. This last view has much in its favour. The peculiar geographical limitation of the disease, its seasonal prevalence, the almost complete immunity of native races, all favour this idea. In these and other respects it seems to be on all

fours with the Texas fever (hæmoglobinuric) of cattle. We know that cattle bred within the endemic area of this disease rarely exhibit the specific symptoms, but that cattle coming from an immune district on entering the endemic area are readily attacked. This is exactly what happens in regard to black-water; the native African is hardly ever affected, whereas the European coming from outside the endemic area is frequently affected. The connection of black-water fever with the malaria parasite seems to have received a parallel in Edington's observations in cattle salted to Texas fever. This talented observer found that such cattle, although originally free from the symptoms of Texas fever, when inoculated with rinderpest frequently developed hæmoglobinuria and exhibited in their blood the parasite (*Pirosoma bigeminum*) of Texas fever. It may be, therefore, that the malaria parasite takes the place in the development of black-water in man that the rinderpest infection in the case of Edington's experiments took in the determination of black-water in cattle.

Hill showed that out of 45 deaths from malaria in Georgetown, British Guiana, from June, 1893, to June, 1895, in persons born in the colony, 31 were under 13 years of age, and only 3 over 21, and in two of the latter the evidence was only clinical. Daniels, in a long series of post mortems from 1893 to 1895, also made in Georgetown, British Guiana, showed that in the series 1289 were born in the colony, or were from other malarial countries. In these 1289 post mortems, pigment (malarial) was found in none under a month old, but was present in those over a month and under 12 months in 25 per cent.; over 1 year and under 2 in 54·5 per cent.; over 2 years and under 5 in 81·4 per cent.; whilst above 30 it was found only in 17·9, 14·1, 13·2, 11·1, and 11·6 per cent., that is decreasingly in each ascending decade respectively. He also noted that after 20 the pigment is very rarely recent in appearance, and after 30, with one or two exceptions, that it is obviously very old. The conclusion

was drawn by Daniels that immunity is acquired by a class in this malarious district in the course of exposure for some 20 years to the infection and, from evidence based on its relative frequency—evidence persisting for considerable periods, in some cases for years,—that this immunity is probably acquired through previous attacks.

What Daniels first proved from observations on a product of the parasite, long afterwards Koch, Christophers and Stevens proved from observations on the parasite itself. They have shown that in the endemic area of malaria practically all native children harbour the parasite. Native children, therefore, are an especially important source of infection. The practical interference therefrom is, that in malarial countries native houses and villages should be carefully avoided.

The most valuable outcome of the recent discoveries in the ætiology of malaria is the enormous power they place in our hands in regard to the prophylaxis of this disease. As the mosquito is a necessary element in the cycle of the parasite, it is manifest that if there are no mosquitoes there will be no malaria; therefore, wherever practicable, mosquitoes should be destroyed. This can be done to a limited or to a considerable extent according to circumstances, at all events in settled districts, by draining, or filling in, or poisoning all such collections of water as the mosquitoes frequent. As the parasite is introduced into man by the bite of the mosquitoes, it is evident that if this bite were avoided malaria would never be contracted; therefore it is of importance to advise and to use means for protecting the human body from the bites of these insects. Then, as quinine kills the parasite, or rather represses it, in the human body, wherever practicable it is advisable to keep the source of the infection of the mosquito at bay by the free use of this drug. In practice some of these measures will be found applicable in one place and some in another. It would be unwise to give general rules for every place; local circumstances must determine which method or methods

of prophylaxis are especially suitable and should be employed. It must be borne in mind that although complete protection everywhere and to every case may be impracticable, relative protection is always possible, should be attempted, and must be of immense value. It is evident, for example, that if in a given district only one mosquito in a thousand is infected with the malaria parasite, and that if in this district a man allows himself to be bitten, say through carelessness in the use of mosquito nets, by ten mosquitoes each night, in the course of a year he will be bitten from three to four times by infected insects. He will therefore be liable every year to frequent reinfection. Whereas if the same man, by exercising a fair amount of care, reduced the number of bites to one a week, he would be bitten by only fifty-two mosquitoes in the year, the probability being that none of these is infected; so that he might pass ten, twenty, or even thirty years in a malarial country before he contracted the disease. Relative protection as against malaria is therefore of immense value, just as is that afforded by vaccination against smallpox, or a good water-supply against typhoid.

As a contribution to popularising the knowledge now acquired that malaria is conveyed by the mosquito, and that it can be prevented by simple methods, methods that are quite compatible with active life, the experiments about to be described by Dr. Sambon were devised. It is right to mention that these experiments were rendered possible only by the intelligent appreciation of the possibilities of modern medicine, and of its importance as a factor in colonial development, by Mr. Chamberlain.

DESCRIPTION OF PLATE XXII.

On Recent Advances in the Knowledge of Malaria (Dr. Patrick Manson).

Fig. 1.

Development of *Coccidium schubergi*.—1. Sporozoit enters epithelial cell and commences the asexual, eimeria, or endogenous cycle. 2 and 3. Development of the schizont. 4. Multiplication of nuclei. 5. Daughter-nuclei arrange themselves at the periphery of the schizont. 6. Formation of merozoits. 7 ♀ and 7 ♂. Female and male merozoits entering fresh epithelial cells, 8, and commencing the sexual, exogenous, or coccidium cycle. 7*b*. Merozoit destined for the renewal of the endogenous or eimeria cycle. 9 and 10. Development of the female (macrogamete) and male (microgamete) gametes. 11. Maturation of the macrogamete by expulsion of caryosome. 12. Multiplication of nuclei and their peripheral arrangement in the microgamete. 14. Development of microgamete. 13. Fertilisation of macrogamete. 15. Fusion of male and female nuclei, encapsulation and formation of oocyst. 16 and 17. Division of nucleus. 18. Formation of four sporocysts. 19. Formation of two sporozoits in each sporocyst. 20. Sporozoit on its way to enter epithelial cell and renew endogenous cycle.

Fig. 2.

Development of *Hæmomenas præcox*.—*a*. Blood-corpuscle into which a spore or a sporozoit has just entered and commenced the endogenous cycle in man. *b* and *c*. Growth and pigmentation of the amœbula in the blood-corpuscle. *d*. Formation of sporocyte. d^1 and d^2. Female and male spores about to enter blood-corpuscles in preparation for the exogenous, sexual phase in the mosquito. d^3. Spore destined to enter blood-corpuscle and renew the human or endogenous phase. *e* and *f*. Female and male gametes in blood-corpuscles; they have assumed the crescent shape and await ingestion by the mosquito. *g*. Female gamete (macrogametocyte) having been ingested by the mosquito has assumed the spherical form. *h*. Male gametocyte, after ingestion by the mosquito, has projected microgametes, *j*, which, breaking away, impregnate the female gamete, *i*. *k*. Zygote (fertilised macrogamete) on its way to the stomach wall of the mosquito—"travelling vermicule" stage. *l*. Encapsulation of zygote in stomach wall of mosquito, and formation of zygotomeres. *m*. Formation of sporozoits or blasts on surface of zygotomeres. *n*. Rupture of capsule and escape of sporozoits into mosquito's body cavity. *o*. Sporozoits on their way to human blood-corpuscles *viâ* the mosquito's salivary gland and proboscis.

Fig. 1.

COCCIDIUM SCHUBERGI

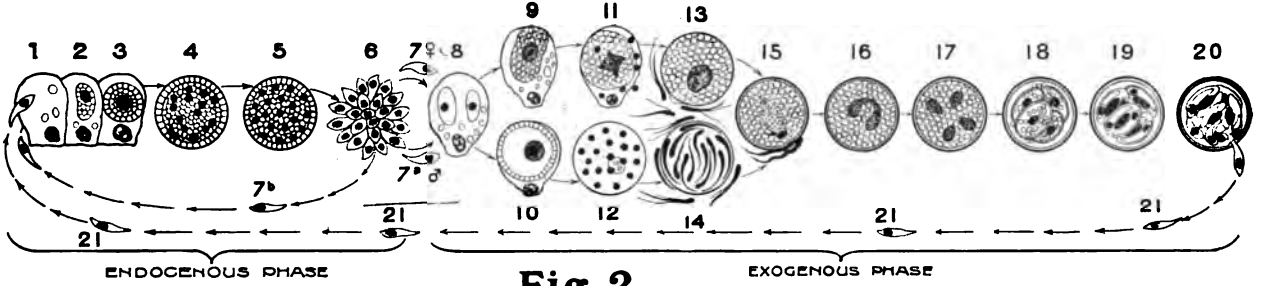
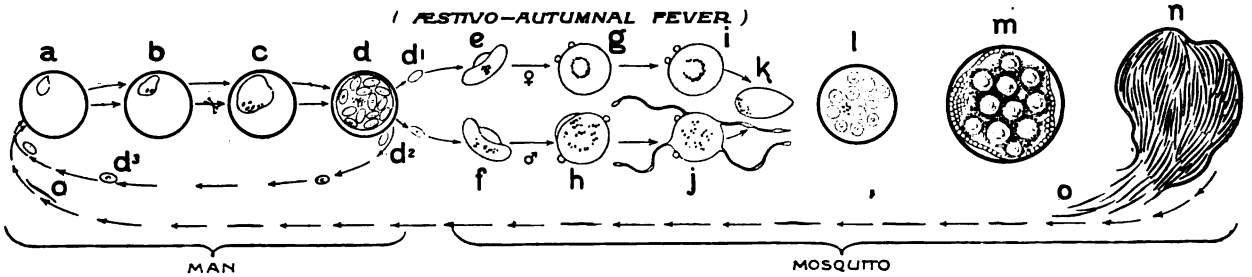


Fig. 2.

HÆMOMENAS PRÆCOX

(ÆSTIVO-AUTUMNAL FEVER)



Bale and Danielsson, Ltd.

REPORT ON TWO EXPERIMENTS

ON

THE MOSQUITO-MALARIA THEORY

INSTITUTED BY

THE COLONIAL OFFICE AND THE LONDON SCHOOL OF TROPICAL MEDICINE

BY

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THE MOSQUITO-MALARIA THEORY.

THAT there might be some connection between mosquitoes and the intermittent fevers peculiar to certain swampy regions was to all appearances a popular belief amongst the ancients, just as it is at the present day in Italy, in the southern Tyrol, and amongst certain tribes inhabiting intensely malarious areas within the tropics. It is, therefore, a mistake to attribute the mosquito-malaria theory to Lancisi, Nott, King, Laveran, or Bignami; these men merely supported the old belief with that power of conviction which they had derived from a wide and enlightened experience of malarial epidemiology.

The discovery made by Manson twenty years ago that a mosquito is the intermediary host of *Filaria Bancrofti*, Cobbold, and the more recent discovery by Smith and Kilborne that *Piroplasma bigeminum* is propagated by a common tick of cattle, the *Rhipicephalus annulatus*, added to the mosquito-malaria theory the support of analogy.

It is to the combined efforts of Manson, Ross, Grassi, Bignami, and Bastianelli that we owe the scientific demonstration of this theory.

Manson pointed to the fact that the flagellation of gametes occurred only in abstracted blood, as indicating the probability of an exogenous cycle in the life-history of the malaria parasites within the body of some blood-sucking alternative host, and suggested that the mosquito might probably be the definitive host of these parasites, because of its wide geographical distribution, of its habits, and of its limitation to swampy areas. He further suggested that possibly each kind of malaria parasite might require a special species of gnat as its alternative host.

Ross, following up Manson's suggestions, discovered that certain mosquitoes were indeed the definitive hosts of the malaria parasites, and that they contracted and transmitted the infection directly by means of their bite. In 1897, he discovered the early encysted form of the æstivo-autumnal parasite within the stomach wall of certain gnats of the genus *Anopheles* which he had previously fed on malaria patients. Being unable to continue his investigations with human malaria, he turned his attention to the *Hæmamœbidæ* of birds, and found in *Culex fatigans*, fed on sparrows or larks containing *Hæmamœba relicta*, zygotes precisely similar to those of *Hæmomenas præcox*, which he had already seen in anopheles.

It remained now to follow out the life-history of the zygotes, and this Ross did with the avian parasites. He saw that they increased in size, divided, and became full of filiform spores, then ruptured and poured out their multitudinous progeny into the body-cavity of their insect host. Finally, he saw the spores accumulate within the

cells of the salivary glands, and discovered that they actually passed down the salivary ducts into the seat of puncture, thus causing infection in a fresh vertebrate host.

Repeating Ross's researches and experiments with the parasites of human malaria and with mosquitoes of the genus Anopheles, Grassi, Bignami, and Bastianelli were soon able to prove that *Hæmamœba malariæ*, *Hæmamœba vivax*, and *Hæmomenas præcox* go through precisely the same transformations as *Hæmamœba relicta* within the body of their respective insect hosts.

The assertion made by Grassi that he had arrived at the demonstration of the mosquito-malaria theory quite independently of Ross's researches led to some misunderstanding as to the priority of the discovery; but, if some of the Italian papers attributed to Grassi this discovery as well as the invention of mosquito-netting, it can be positively stated that no such misunderstanding prevails amongst men like Marchiafava, Celli, Bignami, and Bastianelli, all of whom have given full credit to Ross's work.

The part taken by the Italians in the investigation and elucidation of the mosquito-malaria theory is certainly an important one, and the promptness and ability which they have shown in grappling with the consequent all-important question of prophylaxis is really admirable.

The first in the prophylactic field was Prof. Celli, who, in 1899, started a series of experiments to test the best methods of protection against the malaria-bearing mosquitoes.

Previous Experiments.

The experiments made by the Italian physicians were quite conclusive, and proved beyond doubt the correctness of the mosquito-malaria theory as regards the parasites of human malaria. However, as a means of carrying full conviction to the mind of the general public throughout

the world, they offered some disadvantages. The experiments made by Bignami, Bastianelli, and Grassi to prove that the malarial fevers are transmitted by the means of mosquito bites were carried out in the city of Rome, which, although now usually free from the disease, is nevertheless in the very heart of an intensely malarious region. And those made by Celli were invalidated by the fact that the people placed under protection had suffered from malaria in previous years, and that quinine was administered to them as a prophylactic. The object of Celli's experiments was not to prove that by avoiding the puncture of mosquitoes it was possible to escape fever, but to investigate all such means as might be destructive to mosquitoes, prevent their becoming infected, and protect from their bite.

Object of the Experiment.

For these reasons, and on account of the great importance of the question to the welfare and prosperity of most tropical colonies and protectorates, the Colonial Office decided to make an experiment, which, carried out on strictly scientific lines, might prove in the most convincing and striking manner the truth of the mosquito-malaria theory, and show how far the necessary protection might be consistent with the ordinary avocations of life.

The experiment was suggested by Dr. Manson, and supported by the London School of Tropical Medicine. It was to consist of two tests which should prove the theory, one in a direct positive manner, the other by negative inference. Should they both succeed, no argument could be reasonably brought against the correctness of the theory.

For the first test, a man who had never suffered from malaria, and who had never been abroad, should allow himself to be bitten by mosquitoes reared and infected abroad, and then sent to London.

For the second test, two men who had never suffered

from malaria should go to one of the regions best known as undoubtedly and severely malarious, and should live there throughout a fever season with no other protection than such as might prevent the bite of mosquitoes. For the purpose they would be provided with a mosquito-proof hut.

In a lecture delivered at the Colonial Institute on the 13th of March, 1900, Dr. Manson announced the approach of these experiments, and ventured to prophesy that the man bitten by the infected mosquitoes sent from abroad would contract the disease, whilst the two men living in a very hotbed of malaria, but protected against the bite of mosquitoes, would escape.

Manson's own son, Mr. P. Thurburn Manson, volunteered for the first test, and the second one was entrusted to ourselves.

It was decided to make the second experiment in the Roman Campagna, a district so well known as the classic land of malaria, not only on account of the ravages of the endemic, but also because of the noble work accomplished by the Romans during their long struggle with the disease. Moreover, in the Campagna, the experiment could be closely watched, as indeed it was. It had the further advantage of comparative proximity to London, a circumstance necessary for the first experiment.

In the Roman Campagna, the true fever season usually begins in July, and lasts till the autumn rains, which occur about the middle of October. It was arranged, therefore, that everything should be got ready for the experiment to commence by the end of June. The choice of a suitable locality, the many formalities necessary before the ground could be occupied, and the difficulties of getting a sufficient number of skilled workmen for the erection of the hut, made it impossible to begin the experiment before the middle of July. However, this delay was of little consequence, because the fever season was also delayed on account of unfavourable meteorological conditions.

The month of June was chiefly spent in visiting various parts of the Campagna in order to study the country, the habits of its people, and the conditions favourable or inimical to the malarial endemic. In the many excursions, various kinds of animals were collected, and their blood examined for such parasites as might tend to throw light on those of human malaria. At the same time, the rearing of mosquitoes for the inoculation experiment, and the arrangements most suitable for their transport to London, received all possible attention.

Conferring Malaria by Mosquito Bite.

The first batch of mosquitoes sent to London was reared from the egg in Prof. Bastianelli's laboratory in the Santo Spirito Hospital. The insects were fed on a patient suffering from benign tertian fever, and sent to London on the 29th of June. The case on which the mosquitoes were fed was selected by Prof. Bastianelli, who had found a few tertian gametes in its blood two days previously. On the actual day of feeding we examined several slides of the patient's blood, but failed to find any parasites. However, the mosquitoes were forwarded more to test the efficiency of the method of transport than with any great hope that they would confer malaria.

After that date, owing to difficulties in getting the required number of laboratory-reared mosquitoes when wanted, Bastianelli's assistant went to Porto and collected a large number of young Anopheles which had only just emerged from their pupal cases, and had not fed, to use for the experiment. Although assured that mosquitoes thus collected had already been successfully employed for inoculation experiments by the Italian physicians, we stopped the forwarding of the insects until we had thoroughly satisfied ourselves that we could easily and certainly distinguish the newly emerged and unfed imagines from those which had already fed on blood or plant juices. Having ascertained this to be the case, it

was decided to employ the insects thus collected whenever it was found impossible to obtain laboratory-reared specimens. All the Anopheles sent home after the first lot were collected in the imago stage on the margins of the Porto swamp, which had been at one time the famous hexagonal dock built by the Emperor Trajan. These Anopheles were all of the species *maculipennis*, and each single insect was carefully examined by ourselves. They were all infected on cases of benign tertian fever, this type of malaria being selected because it offers no real danger, and is easily cured by quinine. The patients employed for the experiment were very carefully and repeatedly examined by Prof. Bastianelli, Dr. Panichi, and ourselves, so as to absolutely exclude the possibility of confering any other type of malarial infection.

The second batch of Anopheles was sent to London on the 23rd of August. It numbered twelve insects, some of which had been fed twice or three times on the same patient, a boy suffering from a double benign tertian infection with numerous gametes in the blood. The third batch, numbering fifty specimens, was sent to London on the 7th of September. About thirty of these mosquitoes had been fed on a case of benign tertian. The others, which had refused to bite, were placed in a separate tube labelled "non-infected," and were also sent for control experiments, or to be infected in London if a suitable case offered.

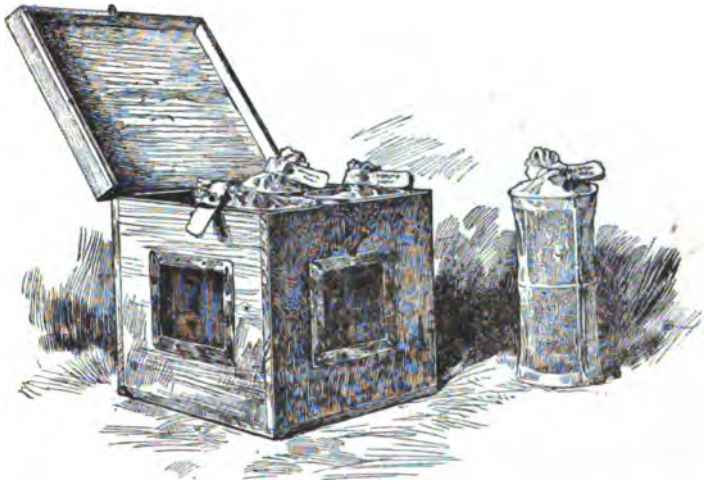
Method of Packing and Transmission.

The transmission of the infected mosquitoes from Rome to London was a matter of some difficulty. The insects had to be kept a certain time until they had been fed on a suitable patient, then they had again to wait in readiness for the Indian mail from Brindisi, the use of which had been kindly permitted by the Post Office authorities. As soon as notice reached Rome of the arrival of the mail at Brindisi, a servant of the British

Embassy in Rome carried the insects along with the Ambassador's despatches to Ancona, where they were delivered to the officer in charge of the mail. An attendant of the London School of Tropical Medicine met the mail at Charing Cross and conveyed the insects to their destination. The journey from Rome to London lasted about three and a half days. So many unfavourable conditions of temperature, shaking, etc., having to be experienced on the journey, it was necessary to devise some apparatus that would obviate as much as possible these risks. It was at first proposed to send the Anopheles in glass tubes, with cotton netting over the top to allow of the transmission of air; but this did not seem a suitable means of conveyance on account of the shaking and jolting to which they would certainly be exposed. Having noticed in our many visits to the houses and stables in the neighbourhood of Ostia that the Anopheles there collected very often, and seemingly by preference, rested on the old cobwebs, and maintained their position on these delicate structures with ease even while the latter were wafted about by fairly strong currents of air, we thought it advisable to reproduce in our arrangements for transmission as far as possible a similar condition. Mosquito netting was loosely applied round a framework of tinned wire, so as to form a cylinder eight and a quarter inches long by three and a half inches in diameter, which might be closed at both ends by means of strings. Four such cylinders were placed within a square wooden box to protect them from damage, to render them more portable, and to keep the insects in a state of semi-obscurity. On each one of the sides of the box was made an opening three inches square, covered with wire netting to allow of the transmission of air, and also to prevent the mosquitoes escaping should the cotton netting in any way get torn. By means of this method of packing, with very few exceptions, most of the mosquitoes arrived in London alive and in good condition. All the mosquitoes that chose were allowed to feed again on the day of departure, so as

to keep them in as good a state of nourishment for the journey as possible. As a precautionary measure, especially for those that had not fed on the day of

FIG. 1.



Dr. Sambon's travelling cage for mosquitoes.

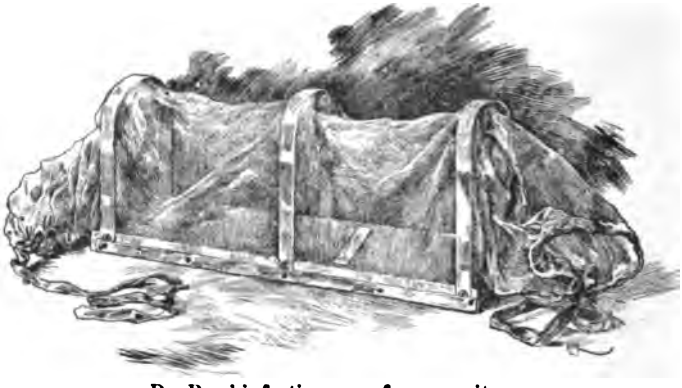
departure, slices of fruit (plum, apricot, or water-melon) were placed beneath each cylinder in such a way that the insects might, if they chose, suck up the juices through the meshes of the netting.

METHODS OF INFECTION.

The aforementioned gauze cylinders were devised simply for the transport of the mosquitoes, and were not large enough to allow of the introduction of the hand. Therefore Dr. Rees, Superintendent of the London School of Tropical Medicine, devised a special apparatus to allow the insects to puncture the man to be experimented upon. To a wooden board on which the hand and arm could be applied, a cradle of cotton netting supported by thin strips of metal was fixed, and the Anopheles liberated inside it. However, as some of the mosquitoes might escape or be killed on withdrawal of the hand, it was

found, on account of the comparatively small number of infected mosquitoes available, that the best method was to place the cylinders in which they had travelled on the

FIG. 2.



Dr. Rees' infecting cage for mosquitoes.

hand or arm of the subject, and thus to allow the insects to puncture through the meshes of the netting.

P. THURBURN MANSON'S CASE.

Mr. P. Thurburn Manson, who had volunteered to be bitten by the infected mosquitoes on their arrival in England, submitted to the puncture of the three different batches. The first batch turned out to be non-infected, as we had supposed from the absence of parasites in the blood of the patient on whom they had been fed; but the second consignment proved successful, and Mr. Manson passed through a sharp attack of double benign tertian fever. Careful notes on the experiment were taken by himself, and are here given *in extenso*.

NOTES OF EXPERIMENT *by* P. THURBURN MANSON, *Guy's Hospital.*

"I am twenty-three years of age, was born in China, but have lived in this country since I was three; have never

been abroad since, nor in any district in this country reputed to be malarial. I am healthy.

The first consignment of mosquitoes arrived at the London School of Tropical Medicine on July 5th. They were in a languid condition, and would not feed satisfactorily. One may have bitten me. By July 7th they were all dead.

The second consignment arrived on August 26th. On arrival twelve insects were lively and healthy-looking. I fed five of them on August 29th, three on August 31st, one on September 2nd, and one on September 4th. They bit my fingers and hands readily. The bites were followed by a considerable amount of irritation, which persisted for two days.

The third consignment arrived on September 10th. There were some fifty to sixty mosquitoes in good condition. Twenty-five bit me on September 10th, and ten on September 12th.

Up till September 13th I had been perfectly well. On the morning of the 13th I rose feeling languid and out of sorts, with a temperature of 99° F. By midday I was feeling chilly and inclined to yawn. At 4.30 p.m. I went to bed with severe headache, sensation of chilliness, lassitude, pains in the back and bones, and a temperature of 101·4°. Repeated examinations failed to discover any malaria parasites in my blood.

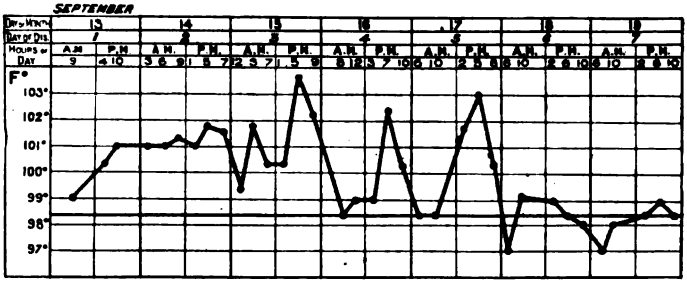
September 14th.—I slept fairly well, but woke at 3 a.m. with slight sweating and a temperature of 101°. During the day my temperature ranged between 101° and 102°. The symptoms of September 13th were exaggerated, and anorexia was complete. Several examinations of the blood were made again with negative result. To relieve headache 10 grs. of phenacetin were given at 6 p.m.; I perspired profusely but slept indifferently.

15th.—Woke at 7 a.m. feeling distinctly better, with a temperature of 100·4°. No malaria parasites were discovered on repeated examinations of my blood by my

father. About 2 p.m. I commenced to feel slightly chilly; this soon wore off, and I became hot and restless. By 4.30 p.m. temperature was 103·6°. It remained about 103° till 9 p.m., when profuse sweating set in. I am told there was some delirium.

16th.—I woke at 8 a.m. feeling quite well; temperature 98·4°. I made several blood examinations, and found one doubtful half-grown tertian parasite. In the afternoon and evening there was a recurrence of fever (temp. 102·8°), relieved by sweating.

17th.—Again felt quite well on waking after a good night's sleep; temp. 99°. At 10 a.m. several half-grown parasites, a gamete, and two pigmented leucocytes were discovered in the first blood film examined. During the



day many tertian parasites were found. Their presence was verified by my father, Dr. Frederick Taylor, Lieutenant-Colonel Oswald Baker, I.M.S., Dr. Galloway, Mr. Watson Cheyne, F.R.S., and Mr. James Cantlie, some of whom saw the films prepared.

About 2 p.m. the sensation of chilliness returned. Temp. 101·8°. By 5 p.m. temperature had reached 103°. There was then copious sweating. The edge of the spleen could be felt on deep inspiration, and there was a slight feeling of discomfort in the region of that organ. Dr. Frederick Taylor and Mr. Watson Cheyne confirmed the presence of splenic enlargement. By 9 p.m. the temperature had fallen to 99·2°, and I was feeling better. Quinine (10 grs.) was given.

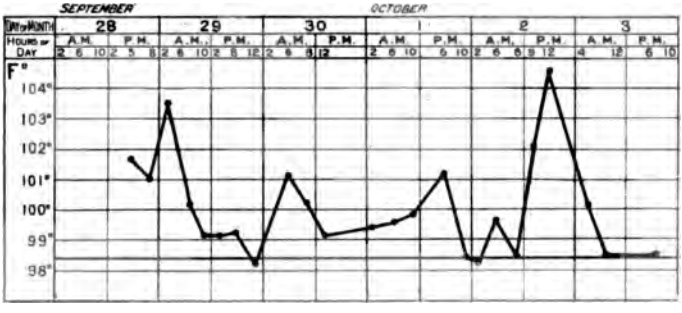
18th.—Woke after a good night feeling perfectly well (temp. 97°). Ten grains of quinine were taken, and subsequently five grains every eight hours. I continued perfectly well all day. A few three-quarter grown tertian parasites and some gametes were found during the forenoon and afternoon; they were seen by Dr. Oswald Browne, my father, and myself. At 10 p.m. the parasites had disappeared, the last being found at 5 p.m.

19th.—No parasites discovered. Temperature normal. Feeling quite well. There is no splenic enlargement and no tenderness. Appetite returned.

25th.—In good health. No recurrence of malarial symptoms."

Warren's Case.

At the same time, Mr. Warren, assistant in the laboratory of the London School of Tropical Medicine, subjected himself to the puncture of the third batch of mosquitoes, namely, those which arrived in London on



the 10th of September. He underwent likewise a severe attack of benign tertian fever. The notes of his case were collected by Dr. Rees, and are as follows:

"Mr. Warren first began to feel ill on Friday, September 28th. The incubation period in his case seems to have been about fourteen days. His temperature on Friday afternoon was 101·6° F., but a careful

blood examination failed to reveal any malarial parasites. The next morning, however, a leucocyte was discovered which contained the characteristic malarial pigment. On Sunday, September 30th, a specimen of his blood was examined, and showed four leucocytes, which contained degenerating advanced pigmented parasites. On Monday, October 1st, he was feeling better, and his temperature was down. That evening, however, the thermometer registered 102°, and at midnight 104·4°. There was no definite rigor, but a distinct feeling of chilliness. The blood examination the next morning revealed young benign tertian parasites; four to six were present in each slide of blood examined. On the following day quinine was administered. The blood specimens in this case were seen by Dr. Manson and a dozen or more of the students working in the laboratory of the school."

Nothing could be more convincing than the history of these two cases in proof of the *rôle* played by mosquitoes in the propagation of malarial fevers. Neither of the subjects of experiment had ever suffered from malaria before; both were residing in a non-malarial country, and both, in consequence of the bite of Anopheles fed on patients of benign tertian in Rome, after a definite incubation period passed through typical attacks of benign tertian fever, and the corresponding parasites were demonstrated in their blood.

Protection from Mosquito Bite.

Choice of Locality.

Whilst these experiments were being made in London to prove that malarial fevers are propagated by mosquitoes, the other and collateral experiment was being carried out in the Roman Campagna. Here four persons were exposed to all those conditions which hitherto had been popularly regarded as causing malarial fevers, and

had no protection except wire netting against mosquito bites.

It had been arranged by Dr. Manson, Prof. Celli, and one of us that the experiment should be carried out at Cervelletta, a low-lying place in the valley of the Aniene, between Rome and Tivoli. This locality, undoubtedly malarious, is now being cultivated by a colony of Lombards, who have already given to a part of the district the appearance peculiar to the rich agricultural districts of their native province. However, when we arrived in Rome, at the beginning of June, we soon became aware that it would have been unwise to erect the hut with which we had come provided, in the Cervelletta district. Firstly, because our experiment would have been looked upon as part of Prof. Celli's experiment, which was being carried out in that locality; and secondly, because Cervelletta was not considered by all to be sufficiently malarious for our special object. We therefore consulted Marchiafava, Celli, Bignami, Grassi, Bastianelli, Gualdi, Dionisi, and other Roman physicians who have made a special study of malaria, and they all agreed that we could not do better than choose either Ostia or Maccarese for the site of our experiment, both places being situated at the mouth of the Tiber, on the low and swampy alluvial soil of recent formation, and both well known as intensely malarious.

We accordingly visited these localities several times, and finally decided to erect our hut in the district of Ostia. A strong point in favour of Ostia was that it would be inhabited throughout the fever season by a number of Ravenna colonists; Maccarese, on the other hand, would be almost entirely deserted at this particular time. The presence of unprotected inhabitants was of great importance to us, because the state of their health would serve as an excellent contrast to our experiment; and, moreover, a number of fever patients in the neighbourhood meant a larger percentage of infected mosquitoes, and therefore greater chances of infection.

Then, again, Ostia was far better known than Maccarese, having been the port of ancient Rome.

In the district of Ostia we chose the locality called Fumaroli, which the inhabitants of Ostia unanimously stated to be the deadliest spot in the neighbourhood. It is about a quarter of a mile to the south of the Ostia pumping station, which since 1890 drains the bed of the old swamp, and was itself the seat of an older pumping station built by Sig. Fumaroli.

The hut was erected on a narrow stretch of ground situated between the new road leading to Castel Fusano and the outlet of the swamp called "Canale dell' acqua salata" (Salt-Water Canal), and bounded on the east by the half-drained swamp which is now thickly overgrown with canes, and on the west by a drainage canal, which discharges the low level waters from the reservoir of the pumping station into the Salt-Water Canal. The area thus circumscribed is at about sea level, and quite six feet below the road, which runs on a kind of embankment. It is entirely formed of sand. The Salt-Water

FIG. 3.

Salt-Water Canal.

Canal, in this part of its course, was at the time of the experiment almost choked by aquatic vegetation, and

behind it rose the pine forest of Castel Fusano, making a most effective background, but adding greatly to the unhealthiness of the place by affording shelter to the adult mosquitoes.

This locality belonged to the State, but was rented by the King, so that we had to obtain permission from His Majesty to erect our hut there. The late King Humbert, with the greatest kindness, at once consented, and showed much interest in the experiment, promising to visit the hut, giving us permission to wander about his hunting preserves, placing his gamekeepers at our disposal, and ordering that every day the state of our health should be reported to him.

That this locality well deserved its bad reputation was fully evidenced by the sickly appearance of the inhabitants, and by the enormous number of Anopheles larvæ in the surrounding drainage canals, in the pools within the pine forest, and especially in that part of the swamp which had been only partially drained in order to serve as a cover for the wild boar and other animals haunting the preserves.

There were only four buildings in the neighbourhood, namely, Castel Fusano, the pumping station, Casa Fumaroli, and Casa Massei.

Castel Fusano itself was uninhabited, but in a neighbouring cottage lived a policeman and two of the King's gamekeepers. These men had all suffered from malarial fevers in previous years. About twelve years ago the bedroom windows of this building had been screened with wire netting by order of Queen Margherita as a protection against mosquitoes and breeze-flies, but only one window still preserved its netting in good condition. The netting had been wrenched from all the other windows long ago to permit the airing of clothes, the growing of sweet herbs, the desiccating of tomatoes, and the many other purposes to which windows are put in Italian households. All the beds were provided with roughly improvised, but fully efficient mosquito curtains.

However, notwithstanding this protection, and the free use of quinine for the slightest ailment, all the inmates of the cottage suffered again this season from slight attacks of fever. The fact is that their means of protection were only nominal; the men used to sit out in the garden during the evening, and were thus frequently bitten by mosquitoes.

FIG. 4.

Reed hut near Ostia. (Drawn by A. Terzi.)

The pumping station is a fine substantial building, with lofty, clean, thoroughly ventilated rooms. It was inhabited during the summer by the superintendent in charge, who went very frequently to Rome, whither he had sent his family and servants. Except when on duty, the workmen slept in the village of Ostia. The superintendent, Sig. Celligari, was a most intelligent and amiable person, who took great interest in our experiment, and

helped us considerably in many ways. He remained to all appearance immune; he had suffered from well-marked malaria in previous years. During the current summer, although he felt ailing and feverish at times, no parasites were ever found in his blood. He made use of a mosquito curtain at night, and took quinine whenever out of sorts. Sig. Celligari was so much struck by the efficiency of our means of protection, that he asked his superiors to provide wire netting protection for the living

FIG. 5.

Old omnibus used as a dwelling near Castel Fusano. (Drawn by A. Terzi.)

rooms at the pumping station; and this being granted, he said that next year he should keep his wife and children in Ostia throughout the fever season. The workmen sooner or later all contracted fever, although they had been several years in the district and had suffered severely in previous years.

Casa Fumaroli was the building nearest to our hut, from which it was distant barely three hundred yards. It was inhabited by seven people, all of whom suffered

severely from malarial fever. They employed no means of protection and distrusted the use of quinine.

The furthest building to the east was Casa Massei, one of the small farmhouses built by the Ravenna colonists. This house provided us with quite a number of patients, because several successive batches of labourers inhabited it at different times, and all contracted fever.

Besides these buildings, there were a few huts in the neighbourhood, and some old omnibuses deprived of wheels and turned into dwellings. The inhabitants of these singular homes suffered severely with the exception of one man, the road-keeper Lupino, who had placed a ridiculously wide netting at the window of his hut, and had made a mosquito-curtain for his bed out of rags of every colour and description sewn together.

With the exception of a few scattered huts and farmhouses, there are no other habitations in the district save the village of Ostia. The latter consists of a few mean buildings clustered round an old mediæval castle, and of three large reed huts, which serve as stables for horses in summer, and as habitations for men in winter.

The population of Ostia amounts to several hundred inhabitants in winter, but dwindles down to about fifty in the fever season. Properly speaking there is no indigenous population in the district of Ostia. With the exception of a few permanent residents, such as factors and innkeepers, the bulk of the population is formed by peasants from various parts of Italy, who come at different times for the various field works. The greater number arrive about the middle of October for the ploughing, the sowing, and the weeding of the land, and leave again in June just before the malarial season begins. These peasants come chiefly from the Abruzzi and from Sora. They congregate in large reed huts very elaborately partitioned, which are thoroughly smoked every evening, and sometimes during the day, by wood fires lighted inside for cooking and washing purposes. Thus, by avoiding the fever season, and by keep-

ing mosquitoes out of their huts, most of these peasants escape malaria unless special meteorological conditions have unduly hastened or prolonged the epidemic.

Two other batches of workers from the Marche and from Umbria come, one in June for the wheat harvest, the other in September for the maize harvest. They sleep in small huts extemporised with boughs and straw, or under a piece of canvas stretched on poles, or in the open without any shelter whatever. These peasants, and especially those who come in September, suffer very severely from malaria.

Of these labourers many have returned to the district for several years in succession, or have worked in other malarious regions, and have therefore suffered previously from fever. But every year there are numbers of newcomers, especially amongst the younger folk, who have never had the disease. These invariably contract malaria after a very short time, which is often not longer than the necessary incubation period.

Of the old cachectics, a few, during some seasons, escape acute manifestations of the disease, as if they had acquired a kind of immunity against the infection. The greater number suffer from attacks of fever season after season, throughout a number of years, as if such immunity did not exist.

Beyond the statement of these facts we have nothing more to say about immunity, because the peculiar conditions of the population of Ostia did not allow of any satisfactory study on the subject.

It has been frequently stated that it is sufficient to sleep one single night in Ostia during the fever season to contract the disease. There was no evidence for such a statement, beyond the somewhat vague and unreliable assertions of sportsmen and peasants. This year, however, soon after the assassination of King Humbert, about fifteen police-agents were sent to Ostia to arrest certain anarchists, who were believed to have taken refuge in that village. On the authority of Prof. Celli, who was

informed of the fact by the police medical officer, we may state that all these police-agents suffered from fever within a fortnight, although they had remained but part of a night in Ostia.

The Hut.

The hut for the experiment was supplied by Humphreys Ltd., London. The building throughout was constructed of yellow fir framing. The whole was erected at Humphreys Ltd. Works, all joints marked, taken down, packed, and delivered at docks for shipment to Rome.

Fig. 6.

British experimental hut.

The building was 32 feet long by 24 feet wide and 3 feet from floor to under side of ceiling, and had an entrance porch 4 feet by 3 feet. The plan consisted of a corridor 4 feet wide through the building, with three rooms on one side, and two large rooms and two small on the other. The foundation provided consisted of timber piles driven into the ground, the top being halved to receive the sleeper plates (six rows being supplied), which in turn carried the floor joists. Upon these the framing of the building was erected. The walls were constructed of 4-inch timber covered on the outside with special rebated weather-boarding with felt lining under, and internally with $\frac{5}{8}$-inch tongued, grooved, and beaded

matchboarding, having an air-space of 4 inches between outer and inner linings. The roof was designed and constructed with overhanging eaves of 3 feet all round, this being required to protect the building from the direct rays of the sun and also to assist the system of ventilation, the 3 feet overhanging eaves being left entirely open, and then covered with mosquito-proof wire. The roof was covered on the outside with 1-inch boarding and tarred felt upon it, the seams being secured with small wood fillets planted on, and when finally fixed covered with a cement composition. All rooms were flat ceiled at 8 feet, giving the whole space of the roof for ventilation, each room having a ventilator 2 feet 6 inches square in the ceiling, covered with wire; thus giving a thorough through current. The floor consisted of 1-inch tongued and grooved flooring, and was finished with a square edged skirting. The windows to all rooms were casements glazed with clear glass, opening inwards. The outside of windows over the whole of the opening was covered with mosquito-proof netting. The entrance doors to porch consisted of one pair 2-inch moulded and panelled doors, the upper panels glazed; and two feet further in the corridor was a partition across same with a single door leading through. All the doors to the rooms consisted of 1½-inch square framed and panelled doors on 1-inch linings, stops, and architraves, all complete.

All doors and windows were painted externally in oil-colour paint. Cast-iron eaves gutter with necessary fascia board was fixed to eaves all round the building, with outlets and cast-iron down pipe complete.

The interior of the building generally was finished in white paint, this being adopted for the easier detection of the mosquito. As an extra precaution, mosquito curtains were provided for each bed; they were placed at a certain distance from the bed, after the manner of a partition,—that is to say, two walls of cotton netting descended at right angles from ceiling to floor, thus

shutting in the corner of the room in which the bed was placed. One side, made of one large piece, was fixed all round by means of strips of wood nailed to the ceiling, the wall and the floor of the room; the other, which served as an entrance, was formed of two pieces hanging in such a way as to widely overlap each other. They were fixed on two sides, and at the bottom were kept closely applied to the floor by means of a weighting shot. The distance of the curtains from the bed prevented the possibility of mosquitoes biting through the meshes of the netting any limb which might be extended out of the bedclothes during sleep.

The cost of the hut, including transport from London to Ostia and erection, amounted to about £300.

At the end of the experiment the hut was presented to the Roman Municipality, which had borne the expense of erection, and had afforded us many other facilities.

In order to secure good drawings of mosquitoes, malarial parasites, and other objects of research, we engaged Sig. Terzi, a distinguished Sicilian artist, who agreed to live with us in the Campagna under the same conditions as ourselves throughout the time of the experiment. As a servant, we employed a man, Silvestri, who, though a native of Rome, had never suffered from malarial fevers. He had been a working naturalist, and proved very useful in collecting material for our work. Thus four people lived in the hut throughout the fever season with no further protection than that afforded by wire netting, and all remained perfectly well throughout the whole time.

This experiment was not only intended to corroborate a fact already scientifically demonstrated, but also to overthrow a number of fallacies and prejudices which prevented the full appreciation of the new discoveries in malaria, and impeded the advantages which would undoubtedly accrue from their practical application. The routine of our life in the Campagna was therefore greatly influenced by the object the experiment had in view. We had to prove that malaria was not carried by a

vitiated condition of the air, as the name of the disease implies, and therefore we always slept with our windows wide open, although the stench of the decaying vegetation and putrefying animal matter from the drying-up canals was very unpleasant at times. The people of the neighbourhood were greatly amazed at what they considered our temerity in exposing ourselves freely to the night air, and many in Ostia who heard of our mode of life would not believe it until they had seen it with their own eyes. To assure themselves on this point several came and walked round our hut in the early hours of the morning. The habit of the Romans of sleeping with hermetically closed windows probably originated on account of malaria, and is, of course, a perfectly consistent one, especially if viewed in the light of our present knowledge of the ætiology of this disease.

The water of malarious localities has also been considered an important vehicle of the disease, and many even now hold that it is so, notwithstanding the negative result of numerous experiments made by Celli, Brancaleone, Zeri and Marino, and the discovery of the *rôle* played by mosquitoes in the transmission of malarial infection.

The only drinking water in our neighbourhood was that of a draw-well in our own compound, and that of a pump-well near the pumping-station. Both supplies were undoubtedly polluted. During the erection of the hut one of us and the servant drank of the muddy well-water nearest our hut, and both subsequently suffered from diarrhœa, which was probably caused by this water. After that, all water from the locality was thoroughly boiled and filtered. However, boiled water was not used long for drinking purposes, because Signor Bisleri, of Milan, kindly presented us with an unlimited supply of his excellent table-water called "Nocera Umbra." The servant, throughout the whole period of our stay in the Campagna, continued to drink very recklessly any kind

of water, even that of ditches and pools, during our long thirsty excursions under the scorching sun of August.

Our food came chiefly from Rome, with the exception of bread, eggs, and sometimes milk and fowls, which were obtained in the neighbourhood. The people of the Campagna attach great importance to the food question in regard to malaria, and therefore it was not to be regretted that the difficulties of our commissariat obliged us to partake of a fare very similar to that of our malaria-stricken neighbours; in fact for a considerable period we messed at the pumping-station with the superintendent in charge.

We never took quinine, arsenic, or any other kind of remedy which might be considered prophylactic as regards malaria.

The turning up of the soil is another condition which has been looked upon as a source of malarial infection, on the erroneous supposition that the germ is capable of saprophytic life. The soil all round our hut was constantly being turned over for a number of reasons, amongst which was that of a possible archæological find. We were encouraged in this hope by the fact that while digging for the foundations of the hut we had come upon a tomb of the time of the Roman empire. It was formed of large terra-cotta slabs, and contained the skeleton of a young woman. Close to the base of the skull was a coin of the Emperor Commodus, evidently the toll-money for the passage of the Styx, which the old Romans used to place in the mouths of their dead. Our subsequent excavations only brought up a rude unfinished marble capital and a few terra-cotta fragments.

Our neighbours were certainly surprised at our immunity and good health, and they watched our experiment with keen interest; but when we advised them to adopt our simple and easy method of protection they shook their heads and invariably answered, "Wait till the rains come." The poor creatures spoke from cruel

experience, because a drenching is always followed by relapse in those who have latent malarial organisms.

When the rains came we went out to see what happened in the Anopheles breeding-grounds, and more than once we were thoroughly soaked by the torrential showers which overtook us in the open country, and the peasants saw us returning home cold and dripping; but no fever ensued, because we had no malarial parasites in our system that a chill might rouse into activity.

Probably for the same reason the inhabitants of Ostia warned us against sea bathing, and certainly the few sunburnt fishermen who spend the livelong day in shallow water collecting shellfish, and who live in miserable reed huts on the beach, suffer terribly from intermittent fevers. The cause of their illness was not difficult to find; all along the shore run parallel chains of sand dunes, amongst which are numerous Anopheles pools.

At St. Michael's Tower, near the mouth of the Tiber, were half a dozen grass huts raised on poles, like the pile dwellings of certain tribes of African and Oceanian savages. They were the habitations of a community of wretched reed-gatherers, who looked pictures of malarial wreckage.

At first we bathed very frequently in the waters of the Mediterranean; but in August and September it was almost worth a man's life to attempt to reach the surf through the pine forest or the jungle, on account of the hosts of breeze-flies which literally swarmed around us. The horses especially suffered terribly from these insects. To protect themselves somewhat from the sting of these flies the horses used to form into circles, with their heads towards the centre. The sight of these rings became very familiar. Sometimes forty or fifty horses were thus clustered in the middle of a field, and there they would stand throughout the hottest part of the day tossing their manes and lashing their long tails all round the circle.

Long experience in the Roman Campagna and in other malarial regions of Southern Europe has taught that the

most dangerous time for contracting malaria is during the evening twilight and at dawn. This fact agrees perfectly with the feeding habits of the mosquitoes of the genus Anopheles peculiar to these regions. We proposed therefore to retire an hour before sunset, and not again to leave our mosquito-proof hut until an hour after sunrise. But we very soon found that it was not necessary to retire so soon as an hour before sunset, because the Anopheles

FIG. 7.

Dwellings of rush-gatherers at the mouth of the Tiber. (Drawn by A. Terzi.)

appeared very punctually a few minutes after sunset and disappeared again a few minutes after sunrise.

During the day we went freely over all the ground within the vicinity of our hut collecting animals and visiting patients. Many people at home and abroad did not hesitate to express their opinion that we should contract fever by exposure in the daytime. Such a risk we soon found was infinitesimal so long as one knew the

danger and guarded against it. At first we were, of course, very careful, because in the interest of the experiment we were obliged to take every possible precaution against mosquito bite, and we made veils of cotton netting to protect our heads, and we wore thick woollen gloves to cover our hands, but very soon we went through woods and jungles unprotected without the slightest fear.

On the 7th of August a military balloon having stranded in the very centre of the swamp, after vain attempts to descend in a neighbouring field so as to avoid being blown on to the pine forest or the sea beyond, we felt obliged to run to the rescue of the aëronauts. Accordingly we entered the thick cane jungle which occupies the half-drained bed of the swamp. For more than two hours we struggled through the canes, which towered several feet above our heads. The heat was unbearable, and when we came out of the thicket with the tattered balloon we were quite exhausted, nevertheless to our surprise we had not been bitten. Had it not been our duty to give assistance, we should never have dared enter that jungle. In fact, up to that date we had carefully avoided coverts.

However, we never sat under cover, especially near pools and ditches, unless we wanted particularly to capture mosquitoes. As illustrative of the improbability of being bitten during the day in the Roman Campagna, we may say that in our many attempts at obtaining specimens of Anopheles peculiar to forests and jungles, we were only able to capture very few specimens.

Although, as a rule, we retired before sunset, still on three occasions one of us was obliged to go to Rome to despatch mosquitoes to London, and on other business, and consequently had to return late in the evening. Each time on the return journey passing through the village was avoided, and a cotton net round the head and woollen gloves were worn. Thus safety was insured, although the drive was for over a mile along

the canal through a veritable cloud of mosquitoes and other insects.

The experiment lasted from the 19th of July to the 19th of October,—that is to say, during the whole of what is considered the season of infection. In fact, the first new cases do not begin before the end of June, and fresh cases after the end of October are exceptional. The length of the season varies somewhat in different years accordingly to the meteorological conditions. Its duration is specially influenced by the earlier or later onset of the autumn rains.

Before our departure already hundreds of people had returned to Ostia; and three days before we left the heavy rains set in.

During the whole time of the experiment, and up to the present day (January 15th, 1901), none of us has had the slightest touch of malarial fever. Dr. Rees, who lived with us for a fortnight in September, and Sig. Gualdi, a medical student, who frequently stayed a night or two with us and kindly helped us in collecting material for our studies, also remained quite well. Our health was perfect during the whole time with the exception of the attack of diarrhœa already referred to, from which one of us and the servant suffered for a few days. As the result of our experiment our health may be said to have improved, notwithstanding the long fatiguing excursions in the Campagna, the great heat and moisture of our encampment, and the poor quality of the food we were able to procure.

During our stay in Ostia we were visited by a number of people; amongst these were the English physicians residing in Rome—Dr. J. Brock, Dr. Burton-Brown, Dr. Eyre, some of the most eminent Italian physicians, such as Prof. Celli, Prof. Grassi, Prof. Bastianelli, Prof. Rossi, Prof. Postempsky, Dr. Gualdi, Dr. Noè, Dr. Foa, and two distinguished German physicians, Dr. Plehn and Dr. Supitza, who had come to Rome for special malarial investigations.

Professor Grassi was so much impressed with the strictly scientific manner in which our experiment was being conducted that he sent the following telegram to Dr. Manson:

"Assembled in British experimental hut, having witnessed perfect health experimenters amidst malaria-stricken inhabitants. Italian physicians congratulate Manson, who first formulated mosquito-malarial theory." —GRASSI.

PHYSICAL CONDITION OF NEIGHBOURS.

The habitation nearest our hut was, as already stated, Casa Fumaroli, at a distance of about 300 yards. In this place lived the Monaldi family, consisting of two men, two women, and three children. All of these suffered repeatedly from malarial fever during the summer, notwithstanding the quinine treatment of each attack. It seemed as if these people were being infected anew again and again. With the exception of one of them, malignant parasites were demonstrated in their blood. They had all suffered in previous years, and showed very evident signs of malarial cachexia. Signora Monaldi had an enormous splenic tumour. The condition of one of the children became so grave that he had to be transferred to the St. Spirito Hospital, in Rome. Casa Fumaroli was always full of Anopheles from the adjacent canals. In the kitchen a number of fowls used to roost at night in a partially closed recess under a stair leading to the bedroom above. This place invariably teemed with fully gorged Anopheles. The women told us that the younger fowls seemed to suffer considerably from bites of these insects, but the blood of such of the fowls as we examined showed no parasites.

Most of the people in our neighbourhood were cachectic, and the peculiar facies of the disease was more or less apparent in all the residents. It was really a pitiful sight to go through the deserted village on a glorious Septem-

ber day and only meet with a few wretched, sallow-faced people closely wrapped in their coarse woollen mantles, who with a tired, absent look tendered us their dry, feverish hands to feel. The contrast between these peasants and ourselves was startling; or between them and the doctors of the malarial ambulances of the Red Cross and their attendants, all healthy and buoyant. The cause of the striking difference in our respective conditions was simply the few yards of wire or cotton netting we used to protect ourselves from mosquitoes. What proof of the efficacy of such means could be better than that supplied by Lupino, the road keeper, who made himself a mosquito curtain of patched-up rags and remained quite well throughout the fever season?

All the unprotected newcomers who remained in Ostia during the summer suffered from severe attacks of fever in the early period of the endemic. Of these, two men who came as factors to the Ravenna Colony were of special interest on account of the good condition of their health at the outset, and the comparatively hygienic circumstances under which they lived. One of these, Signor Francia, was very reckless; but the other, Signor Bonivant, was rather anxious about his health, and took quinine as a prophylactic. Early in July both were attacked with quotidian malignant fever, and were obliged to leave the district for some time.

Several patients came to our hut for quinine or advice, and the Red Cross doctors, especially Dr. Bartera, brought us blood-films from the patients they had found amongst the harvesters and conveyed to the hospital. Thus we were able to examine the blood of about fifty patients. In most cases parasites were easily found, but in some cases parasites could not be demonstrated, doubtless on account of the large doses of quinine which the patients had received from the municipality doctor, the Red Cross doctor, or their employers. In the early part of the season, tertian parasites were usually found, but later the malignant parasites were by far the most prevalent. In

September, a case of quartan fever was detected in a labourer working in the maize fields of Calabresi's estate, but this fever had been contracted out of the district. No other cases of quartan fever came under our notice or were described to us by the doctors or the peasants themselves. Several cases of mixed infection of tertian and æstivo-autumnal parasites were observed. In cases of æstivo-autumnal infection crescent bodies were never found; this may be explained by the fact that the patients who came under our observation were in the early stages of the infection,—that is, at the time when the gametes are not yet present. The crescent bodies seem to appear only after several febrile attacks, when probably the endogenous multiplication of the parasites is opposed through acquired resistance.

Numerous Anopheles were collected from houses, huts, and stables. Many of these were dissected, others were sectioned; very few were found to be infected with malaria parasites. Of fifteen collected one day from Casa Fumaroli, at a time when the inmates were suffering most from malaria, only two were found to have parasites, and these were in the early stages of development. However, we do not think that our observations on this point were sufficiently numerous to allow of any definite statement as to the relative number of infected insects. The Anopheles do not seem to remain long in rooms in which they are likely to be disturbed. Their number in the same varied very greatly from day to day.

The Mosquitoes of the District.

Our studies as regards the mosquitoes of the district were principally limited to those of the genus Anopheles. Of these, only two species were found, namely, *A. maculipennis* and *A. pseudopictus*. Although *A. bifurcatus* is said to be found in the locality, we did not come across a single specimen.

A. maculipennis (syn. *A. claviger*, *A. quadrimaculatus*

Pl. XXI, figs. 1—3, and Pl. XXII, fig. 3) is by far the commonest Anopheles of the region. Like *Musca domestica* and other insects, it has linked itself with man, and is now found in all the houses and stables placed in the neighbourhood of its breeding grounds. It is therefore, without doubt, the chief propagator of the malarial fevers of the region. Its larvæ were found in almost every water collection, from the broad outlet of the swamp to a small tub half full of water near the pumping station. The region is being partially reclaimed, and is intersected by a vast system of drainage canals, which during the summer were stagnant and overgrown with aquatic vegetation. Larvæ of Anopheles were found in the majority of these canals, especially on the leeward side of bridges.

At first we thought that the larvæ found in the Salt-Water Canal had probably drifted into it with the current, because they were chiefly found amongst a veritable *sargasso* of floating weeds close to the leeward bank. But a more careful observation showed that this was not the case. In fact, there was no current of water in the canal during the summer, because the mouth of it was entirely blocked up by a wide extent of sand, which had been thrown back by the sea. Moreover, the little shallow bays and pools made by the union of clumps of reeds along the banks of the drying-up canal were all plentifully stocked with newly hatched larvæ. In the brackish water near the closed-up mouth of the outlet, amongst large brown clumps of floating algæ and seaweed, Anopheles larvæ were very plentiful. Here, most of them were of a dark colour, some being jet-black, with milky white spots on one or more segments along the back.

In pools entirely covered by duckweed (*Lemna*) Anopheles larvæ were never found (Fig. 8).

In a pool within the pine forest of Castel Fusano, and in some pools and ditches within the cane jungle beside it, we also found larvæ of *A. pseudopictus*. The distinction between the larvæ of *A. maculipennis* and those of *A.*

FIG. 8.

Pool entirely covered by duckweed, and consequently free from Anopheles larvæ. (Drawn by A. Terzi.)

FIG. 9.

Anopheles pool in pine forest. (Drawn by A. Terzi.)

pseudopictus was quite easily made out with a low magnifying power by applying Grassi's test, and was confirmed by rearing the imagines of both species from the larva.

Anopheles larvæ in all stages of development were constantly found from the beginning of June to the end of October, thus showing a continuous irregular succession of generations.

The number of larvæ in the different pools and at different times varied greatly without apparent reason. A striking instance of this was that of a small pool in Castel Fusano, close to the wooden hut in which King Humbert used to have his luncheon when out shooting. On the 20th of September, this pool contained absolutely no larvæ either of Culex or of Anopheles, but a fortnight later it was found to be simply teeming with both in all stages of growth, and on its surface were floating innumerable Culex egg-masses.

After torrential rain the number of larvæ remained almost the same in those pools which were under cover of trees and were not liable to be scoured out by the rain, on account of the depth of their banks, but they diminished somewhat in the smaller shallow pools in more open places, and almost entirely disappeared from the outlet after its mouth had been opened and a strong current established by means of the accumulation of water due to the rain and to the pumping operations.

In all the pools and canals were enormous numbers of frogs, besides swarms of larvæ of dragon-flies and water-beetles. The outlet and the wider canals contained, moreover, several species of fish, amongst which the young of grey mullet (*Mugil cephalus*) were innumerable, but the Anopheles larvæ occupied the shallows at the edge of the stream, where they were greatly protected by the dense aquatic vegetation.

Wishing to test the relative value of natural enemies as regards the destruction of mosquito larvæ, we made a few experiments with the larvæ of various water-beetles and other insects, and we found that the larva of a very

common and beautiful species of dragon-fly (*Crouthionis erythrea*, Pl. XXII, fig. 1) was especially deadly to mosquitoes. The odonata larvæ when provided with Anopheles larvæ in small glass vessels certainly devoured a considerable number of the latter. Such experiments, however, are of little value, as they do not reproduce the natural conditions. In fact, it cannot be said that the larvæ of this dragon-fly would not have taken other food by preference in their natural breeding grounds, as is most reasonably suggested by the size of their curious prehensive organ usually called a mask. The fact was certainly evident that enormous numbers of mosquitoes reached their adult stage, notwithstanding the extreme abundance of their natural enemies.

No experiments were made with larvicides, but we are convinced that the vast extent of ground covered by innumerable pools, swamps, and canals, usually thickly overgrown with aquatic vegetation, offered such difficulties that any attempt of the kind would have been hopelessly futile. Undoubtedly there are collections of water suitable to the kerosene treatment, especially in the neighbourhood of habitations, but many of these could preferably be filled up, drained, or stocked with small fish.

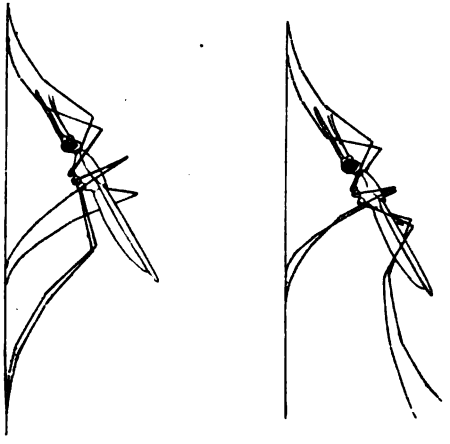
A most important matter in the abolition of mosquitoes is the clearing of canals and streams from water weeds, which offer the best breeding conditions. In the Roman Campagna and in the Pontine Marshes the wider canals are cleared by means of herds of buffaloes, which are driven into the stream and followed by men in punts, while other men with dogs run along the banks to prevent the buffaloes from landing.

As already mentioned, *A. maculipennis* was found in great numbers in the houses, chicken coops, and stables, in the last places often resting on the old dusty cobwebs which heavily curtained the ceilings. In the houses they chose the darkest corners, often resting under tables, beds, and chairs, but more frequently on the ceilings,

especially when these were blackened with the smoke of winter fires and well out of the way of danger. In the rooms of an inn which had a blue stripe all round their whitewashed ceilings, the Anopheles seemed to settle by choice on the dark stripe.

A. maculipennis usually, when resting on a vertical surface, sits at an angle of about 30°, the angle, however, varying slightly according to the position of the legs, the development of the ovaries, and the state of engorgement. Although this angle is much wider than that assumed by the local species of Culex, it is certainly not sufficiently marked to enable anyone to recognise the genus at a

FIG. 10.



Resting position of *Anopheles maculipennis*.

glance. A really characteristic difference between the Culex and Anopheles genera is that pointed out by Mr. Waterhouse. In Culex the head and thorax form an angle with the abdomen, which gives the insect a curious hump-backed appearance; in Anopheles the head, thorax, and abdomen are almost in a straight line.

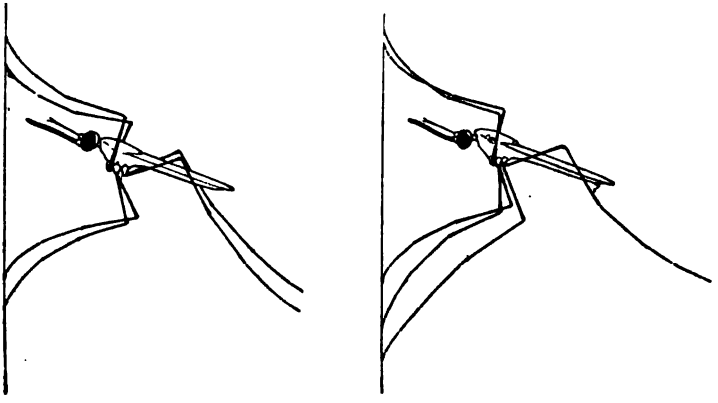
Having reared adult specimens of *A. pseudopictus*, we observed that they sit on a wall at a much wider angle than *A. maculipennis*. In fact, the body and the support

usually form an angle of about 70°, at times attaining almost 80°.

As some importance has been given to the resting attitude as a means of distinguishing the genera Culex and Anopheles, it is well to state that this distinction has no value in the diagnosis of genera, although it may be very useful in distinguishing species.

In the month of July adult specimens of *A. maculipennis* were very abundant, and continued so till the middle of September, when four days of torrential rain greatly diminished their numbers. After this, however, the number again increased, and remained fairly constant till the middle of October, when the weather became cooler and the autumn rains set in. In July and August no Anopheles were seen round the hut during the daytime, but in September and October, when there were several dull and cloudy days, a few stragglers occasionally appeared about the windows. On the whole, however,

FIG. 11.



Resting position of *Anopheles pseudopictus*.

their times were very constant, the time of appearance being a few minutes after sunset, and that of disappearance soon after sunrise. During the day they probably rested in shaded places amongst reeds or under bridges, etc., but though we often looked for them in such places

we never found them. They were always found in houses, stables, and in a well situated within twenty yards of our hut. From this well we could always secure plenty of specimens for study. Although continually looking for them and disturbing them in houses for the purpose of capture, none of us were ever bitten.

Conclusions.

This experiment has certainly proved beyond doubt that mosquitoes, and only mosquitoes, are capable of transmitting malarial fevers; that protection from their bite implies absolute immunity; that the protection is easily obtained, and does not in any way interfere with the ordinary avocations of life.

The sanitation of malarial regions is now within the pale of possibility. It implies the destruction of mosquito-breeding places in the neighbourhood of habitations by suitable drainage and cultivation, and the education of the people in the *rôle* of the mosquito, and in the prophylactic use of quinine and mosquito netting.

APPENDIX A.

HÆMOCYTOZOA OF ANIMALS.

During our sojourn in the Roman Campagna, we examined the blood of various animals in order to study their hæmocytozoa, and possibly to ascertain whether any of the local vertebrates might foster the endogenous cycle of our malaria parasites, and thus become factors in the epidemiology of the disease.

Already Celli, Sanfelice, Santori, Grassi, and Dionisi had made similar researches in the vertebrate fauna of the Roman Campagna, and had found parasites in the blood-corpuscles of frogs, larks, sparrows, pigeons, owls, oxen, and bats.

Our researches on the subject were somewhat limited on account of the short time we were able to spare for such investigations, and the difficulty we experienced in procuring the necessary material. The people of the locality were for the most part unwilling to let us examine their domestic animals, and, notwithstanding the rewards we offered, gave us no assistance in the capture of wild animals. The animals we were able to examine were captured by ourselves during our excursions. There was a great dearth of mammals and birds in the region, and the hours in which we were able to be about were certainly the least favourable for hunting. However, we managed to examine 188 reptiles, 33 amphibians, 24 birds, and 104 mammals.

Lizards.—Both *Lacerta muralis* and *Lacerta viridis* are exceedingly common in the Roman Campagna. Both offer a great variety of colouring more or less in harmony with that of their special surroundings. *L. viridis* varies in colour from a pale yellowish green with white stripes along the sides of the back, to the most intense emerald-green studded with numerous black spots. *L. muralis* is of a light tawny colour on the yellowish sands along the sea-shore, and of a glossy black colour dotted all over with deep green spots in thick jungle.

We examined 120 specimens of *L. muralis* and 25 specimens of *L. viridis*, and we found *Hæmogregarina lacertarum* in nine of the former and in one of the latter. Celli and Sanfelice,[1] in 1891, examined 100 specimens of *L. muralis* and 20 specimens of *L. viridis*, but failed to find any parasites.

The parasite found in *L. muralis* was no doubt that described by Labbé[2] and called by him *Karyolysus lacertarum*. We noticed the small endoglobular phase and the so-called vermicule phase, which may be contained

[1] A. Celli e F. Sanfelice.—"Sui parassiti del globulo rosso nell' uomo e negli animali," 'Annali di Agricoltura Roma,' 1891.

[2] A. Labbé—"Parasites endoglobulaires du sang des vertébrés," 'Arch. de zoologie expérim.,' Paris, 1894.

within the corpuscle or may lie free in the plasma. We also noticed the large oval bodies with numerous chromatoid granules at the periphery, probably representing early forms of the endogenous multiplication phase (*cytocysts*).

The early endoglobular phase consists of minute round or oval bodies, with very bright granules. These bodies enlarge within the endoplasma of the erythrocyte, and acquire an elongated cylindrical shape, with brilliant granules at the extremities. Usually one extremity tapers somewhat into a point, and gives the parasite a club-like appearance. The parasite is usually placed lengthways parallel to the long axis of the corpuscle, and lies extended; but it may bend round the nucleus, or it may double up on itself. The infected corpuscle soon becomes pale and enlarged; its nucleus is pushed on one side by the growing parasite, and as a rule becomes greatly elongated.

Of the infected specimens of *L. muralis* several had very slight infections, but in three of them there were large numbers of parasites. In a series of twenty very young lizards examined no parasites were detected. The lizards collected at Maccarese were far more frequently infected than those captured in the district of Ostia.

The definitive host of *Hæmogregarina lacertarum*, if there be one, is as yet unknown. On several lizards a small blood-red acarus very similar to *Geckobia latastii* was present, and may or may not have had some part in the causation of the infection. This parasite was usually found on the legs or between the scales of the tail.

The *Hæmogregarina* found in the blood of *L. viridis* did not differ in any apparent way from that found in *L. muralis*.

Ten geckos (*Tarentola mauritanica*) were collected in various houses and examined, but they did not contain any hæmoparasites.

Tortoises.—We also examined eight land tortoises (*Testudo græca*), which were found in the forest of Castel Fusano, but they were not infected. We were not able to obtain any specimens of the fresh-water tortoise (*Emys*

orbicularis) ; but Celli and Sanfelice, who examined several of these animals from the swamps of Ostia and Maccarese, found no parasites in any of them, although they frequently found *Hæmogregarina stepanowi* in tortoises of the same species from Pisa and Venice.

Snakes.—None of the snakes examined (*Zamenis gemonensis, Cornella austriaca, C. girondica, Vipera aspis*) contained Hæmocytozoa, nor did we find any parasites in the blood of twenty-one slowworms (*Anguis fragilis*), some of which were collected at Maccarese, others at Ostia.

Batrachians.—*Hæmogregarina ranarum* and *Hæmogregarina splendens* were both found very frequently in the edible frog (*Rana esculenta*), but no parasites were found in two specimens of *R. agilis*. Ten toads (*Bufo vulgaris*) were also examined, but no parasites were found in their blood.

Birds.—On account of the difficulty experienced in obtaining birds, few were examined.

We found *Hæmamœba danilewskyi* in two out of six pigeons (*Columba livia*) examined. The other birds examined were three jackdaws, two kingfishers, five swallows, three owls, one blackbird, and one sandpiper, but in none of them were parasites found.

Bats.—Dionisi,[1] in 1898, discovered three new hæmocytozoa in the blood of three different species of bats. The first he found in *Miniopterus schreibersii*, and is very similar to the parasite of quartan fever. The second he discovered in *Myotis myotis* (vel *Vespertilio murinus*) ; the parasite of this bat in some of its stages resembles the quartan parasite, in others that of tertian fever. The third was an unpigmented parasite analogous in some of its phases of development to the parasite of so-called æstivo-autumnal fever ; Dionisi found it in the blood of *Vesperugo noctula*.

For the classification of these parasites, Dionisi proposed two new genera, one of which he named *Polychromo-*

[1] A. Dionisi.—"La malaria di Alcune specie di pipistrelli," 'Annali d' Igiene Sperimentale,' Roma, 1899.

philus, because of the different behaviour of the parasites towards Romanowski's stain in their various stages of development; while the other he called *Achromaticus*, because the parasite belonging to this genus never contains any pigment.

To the genus *Achromaticus* belongs the parasite of *Vesperugo noctula*, to which he gave the specific name of *Achromaticus vesperuginis*, and to the genus *Polychromophilus* belong the hæmocytozoa of *Miniopterus schreibersii* and *Myotis myotis*, for which Dionisi proposed the respective specific names of *Polychromophilus melanipherus* and *P. murinus*.

We examined very carefully fifty-eight specimens of *Myotis myotis*, two specimens of *M. capaccinii*, and seventeen specimens of the lesser horseshoe bat, *Rhinolophus hipposiderus*. About twenty of the *Myotis myotis* and one of the *M. capaccinii* were captured in some tufa caves near Ariano; all the other bats were collected in the district of Ostia.

We found no parasites in the numerous specimens of *Myotis myotis* and *Rhinolophus hipposiderus*, but both specimens of *Myotis capaccinii* contained hæmocytozoa corresponding exactly to the *Polychromophilus melanipherus* described by Dionisi as the parasite of *Miniopterus schreibersii*.

Myotis capaccinii, commonly known as the hairy-tail bat, is rare in Italy; it is not found in large clusters like *M. myotis*, but as isolated individuals or amongst the clusters of *M. myotis* and *Miniopterus schreibersii*.

The two specimens of *M. capaccinii* were captured and examined in June; only one or two parasites could be seen in each slide of peripheral blood. These parasites were to all appearances gametes. They were ovoid or roundish bodies, with coarse granules of black pigment, similar to those of quartan parasites, scattered about the cytoplasm in various ways or gathered at its periphery. Some of the parasites seemed free in the plasma, others were endoglobular and occupied almost the entire erythrocyte, which was

thereby somewhat altered in shape, but not appreciably enlarged.

Post mortem many parasites were found collected in the cerebral capillaries, and there were some evidences of a slight pigmentation; no pigment was seen in the liver and spleen, and the latter organ was not enlarged.

Most of the bats were covered with ectoparasites of two sorts, namely, certain Acarina (*Pteroptus vespertilionis*, etc.) and a dipterous insect (*Nycteribia dufourii*, see Pl. XXII, fig. 2), but we were not able to ascertain whether these parasites play any part in the transmission of the infection.

Cattle.—Hæmoglobinuric fever (Texas fever) is by no means an uncommon disease of cattle in the Roman Campagna, but it is far more deadly to herds of imported cattle. The indigenous greyish-white, long-horned stock seems to have acquired a certain degree of immunity. It is only after the heavy and long-continued work of the harvest season that some of the local animals are attacked. These native cattle live in a state of semi-wildness, and have no shelter.

During our stay in Ostia, there occurred five cases of hæmoglobinuric fever, three amongst local cattle and two in imported animals. We were able to examine three of the cases; of the other two one had died and the other had recovered before any news reached us of their sickness.

Case 1 was an indigenous ox. When we called to see it, the animal was lying in a grass field, with the head close to the ground, and in a dull, listless condition, which is very appropriately pictured by the name "tristeza" given to the disease in South America. The animal had been ill for several days, and had been passing red water. It was considerably emaciated, had well-marked jaundice of the scleroticæ, and was so feeble that it was with great difficulty it could totter to its legs. The muzzle was dry and hot, and on passing the hand over the body, a high temperature was very perceptible. While we were examining

it, it passed about one pint of dark port-coloured urine. A large number of ticks were found on its hind legs, and especially round the mammæ. They belonged to different species, *i. e. Hyalomma ægyptium, Rhipicephalus sanguineus*, and *Rhipicephalus annulatus*. A careful examination of blood-films taken at the time revealed the large pear-shaped parasite (*Piroplasma bigeminum*) discovered by Theobald Smith.[1]

The ox died next day, but as the weather was exceedingly hot, and as no information was sent of its decease until the following day, a *post-mortem* examination was deemed useless.

Cases 2 and 3 were two Swiss-Lombard cows which had been recently imported by the Ravenna colonists, and were kept during the summer in Ostia chiefly to supply us with milk. Both cows developed high fever on the same day. They had been feeding in the same field, and inhabited the same byre. On the following day one of them passed redwater.

One of these cows was treated by free bleeding and copious purging, with the result that it died the same day; the other was fortunately left alone, and, though passing through a severe attack of fever with the characteristic emission of redwater, eventually recovered. The large pear-shaped parasite was found in the blood of the latter. Ticks of the species *Rhipicephalus annulatus* and *Hyalomma ægyptium* were found on both cows.

A *post-mortem* examination was made of the dead cow immediately after death, and it showed the following appearances.

The animal was well nourished. The scleroticæ were slightly jaundiced. On opening the abdomen, the peritoneum was found to be markedly jaundiced. The uterus contained a fœtus at the sixth month. The heart contained much dark clotted blood in the right side. The kidneys were slightly congested. The liver was enlarged,

[1] Theobald Smith—"Preliminary Observations on the Micro-organism of Texas Fever," 'Med. News,' December 4th, 1889.

discoloured, and congested. The spleen was enlarged, very much congested, and its pulp almost diffluent. The bladder contained about a pint of wine-red urine, although the cow had not passed any redwater during life. Examination of this urine showed hæmoglobin crystals, but no red corpuscles. Blood smears were taken from the various organs. Microscopic examination of these preparations showed in a large percentage of the red corpuscles the small coccus-like *Piroplasma*. The greatest number of infected corpuscles was found in the smears from the kidney. No parasites were found in the blood of the fœtus. The immunity of the fœtus has already been noticed by Smith and Kilborne[1] in cattle hæmoglobinuric fever, and by Bignami, Bastianelli, and Thayer in human malaria.

In the smear preparations from this case and in the blood-films from Case No. 1, we found certain large, highly refractive bodies of a very definite long ovoid or fusiform shape, with coarse granules of reddish-black pigment collected centrally or scattered throughout the endoplasm. These bodies struck one at first glance as possibly homologous to the crescentic gametes of æstivo-autumnal fever.

In stained specimens of blood from Case No. 1, we also found numerous corpuscles, two or more times the usual size, speckled with a variable number of granules deeply stained by Loeffler's methylene blue. These "punctate cells," first described by Theobald Smith, are in every way similar to the speckled corpuscles found in the oligocythæmia of patients recovering from æstivo-autumnal fever.

An interesting question in the study of cattle hæmoglobinuric fever is that of the relation of the large pear-shaped parasite of the early summer months to the small

[1] Smith, T., and Kilbourne, F. L.—"Investigations into the Nature, Causation, and Prevention of Texas or Southern Cattle Fever," 'Bulletin No. 1, Bureau of Animal Industry, U.S. Department of Agriculture,' Washington, 1893.

coccus-like form which is usually found later in the season. Are they different parasites or only different stages in the life-history of the same organism ?

Theobald Smith inclines to the latter view, because in two inoculation experiments with the blood from cases in which the large pyriform bodies were found, the inoculated animals developed first a similar attack characterised by the same large parasitic form, and later exhibited a return of fever with the small form, although they had been kept away from every possible source of infection.

These experiments are by no means convincing; on the contrary, they are very similar to those experiments made in man which have been so frequently brought forward in support of the now exploded theory of the unity and polymorphism of the malarial organisms of man. Thus, in 1889, Gualdi and Antolisis inoculated two patients intravenously with 3 c.cm. of blood from a patient suffering with quartan fever. In the first case an irregular fever appeared ten days after the inoculation, the blood showing the organisms characteristic of æstivo-autumnal fever. In the second case the inoculation was followed, in twelve days, by a mild irregular fever, the blood showing a few quartan parasites, but also, as in the former case, æstivo-autumnal parasites.

In two cases of cattle hæmoglobinuric fever we found the large pear-shaped parasite alone; in a third case we found the small parasite and not one single large form or any form of intermediate size which might suggest a connection between the two forms.

Our very limited opportunities prevented us from arriving at any definite conclusion, but it is quite possible that the two forms represent distinct species. Both forms seem to multiply by simple binary division as described by Laveran and Nicolle.[1] Now, if the two forms represented merely different stages in the life-history of the same parasite it would be difficult to understand why

[1] Laveran, A., et Nicolle, M.—'Contribution à l'étude de *Pyrosoma bigeminum*,' Soc. de Biologie, 29 juillet, 1899.

this parasite should have two distinct endogenous cycles in the same host, and why the process of multiplication should be exactly alike in both cycles.

The life-history of the small *piroplasma* of sheep and that of the large *piroplasma* of dogs lend to the dual view the support of analogy. In this connection, it is interesting to note that the cattleherds of the Roman Campagna assert that oxen often contract the fever when allowed to graze in fields previously occupied by diseased sheep.

Horses.—On the 8th of July we were called to examine a horse suffering from intermittent fever at the stable of the military-police station in Fiumicino. Two other horses in the same stable had sickened in a similar way about the 20th of June, and both had died. These horses were of Hungarian breed, and had been imported into Italy the previous year. They had been stabled at Fiumicino since the 14th or 15th of April. The horse we examined had sickened on the 26th of June, when its temperature had risen to over 40° C. The officer in charge told us that at first the temperature was irregular, but that later it became decidedly intermittent; there had been a paroxysm on the 4th of July, no fever on the 5th, and then again another mild paroxysm on the 6th. The other two horses had suffered from continuous fever, with a variation of about 1° C. At the same time some of the men in the rooms above had suffered from tertian fever notwithstanding the compulsory prophylactic use of quinine. At the time of our visit, the affected horse had no fever, but was very anæmic and languid. There were no other symptoms of disease. We prepared some blood-films and collected a number of mosquitoes (*Anopheles maculipennis*) which were resting on the walls and ceilings of the stable, and were all well gorged with blood. The stable was in a perfect sanitary condition and scrupulously clean.

On the previous year, also in June, all the five horses stabled at Fiumicino had contracted fever and had to be sent to Rome, where four of them continued ill from

twenty to forty days, and one till the following October.

In examining the blood from the Fiumicino horse, we only found one doubtful endoglobular, unpigmented, vacuolised and deeply stained parasite. The mosquitoes collected in the stable of the diseased horse revealed nothing, but some days later, in a specimen of *Anopheles maculipennis* captured in another horse stable in Ostia, we found in its stomach wall a body exactly like the one we had seen in the horse's blood.

Dogs.—Piana and Galli-Valerio [1] have described a large pear-shaped parasite (*Piroplasma bigeminum*, var. *canis*) in pointers, but we did not find any kind of hæmocytozoa in the dogs of Ostia, although we very frequently examined their blood.

APPENDIX B.

EXAMINATION OF DOGS FOR FILARIÆ.

Filaria immitis is very prevalent in the neighbourhood of Ostia. We found its free embryos in eight out of twenty-one dogs living in the district. It was almost invariably found in the older dogs, many of which showed signs of stiffness, suffered from dyspnœa, and were unwilling to follow us in our excursions.

The limitation of this widely distributed filaria to certain swampy regions led to the belief that its intermediary host might be a crustacean or a mollusc. In 1879, Bancroft believed to have discovered that the intermediary host of *F. immitis* was *Trichodectes canis*, the common dog louse, and Sonsino stated that he had found it in *Hæmatopinus pilifer*, another common ectoparasite of dogs. Later, Sonsino and Grassi incriminated *Pulex serraticeps*, the dog's flea, but further investigations obliged them to abandon this view.

In 1892, Calandruccio found in a mosquito a larval

[1] 'Moderno Zoiatro,' 1895, No. 9.

filaria, and suggested that it might possibly be *F. immitis*, but he did not make any further investigations. At last, in 1900, Grassi and Noè [1] positively established that *Anopheles maculipennis* is an efficient intermediate host of *F. immitis*. They found that the embryos, after ingestion, pass into the Malpighian tubes of the mosquito, there grow, and, after having attained their maximum stage of development possible in the mosquito, traverse the tissues of the insect and reach the labium, eventually escaping by rupture of the same into the next dog bitten.

By feeding mosquitoes of the species *A. maculipennis* on a filariated dog, and then keeping the insects alive for varying periods, we were able to follow out these changes and fully corroborate the observations made by Grassi and Noè, but the few experiments we were able to make do not justify us in accepting the inoculation hypothesis of these authors, which implies the rupture of the filariated labium along its dorsal aspect.

Laboratory-reared mosquitoes were applied to the infected dog by means of test-tubes until they had fully gorged themselves, then they were placed in large cages made of cotton netting stretched over a wooden framework, and kept alive by feeding on the juices of fruit until ready for dissection. When required, the insects were killed, hardened, embedded in celloidin, and sectioned.

Twelve hours after feeding the young filariæ had migrated from the stomach, and were found lying in the Malpighian tubes. From this time onwards they gradually increased in size in a somewhat similar manner to the embryos of *Filaria bancrofti* amongst the thoracic muscles of *Culex pipiens*, and reached a stage in which a well-marked alimentary canal was visible. In sections, ten days after feeding, the filariæ were seen to have reached their maximum stage of development, and some had begun to migrate towards the head. This coincides with Grassi and

[1] Grassi, B., e Noè, G.—"Propagazione delle filarie del sangue esclusivamente per mezzo della puntura di peculiari zanzare," 'Rendicanti della R. Accademia dei Lincei Roma,' 1900.

Noè's experiments. The latter investigators found that the filariæ, in summer, usually leave the Malpighian tubes on about the tenth day, and reach the labium one or two days later.

In sections eleven days after feeding on an infected dog, some filariæ were still within the Malpighian tubes.

In sections of an *Anopheles maculipennis*, from a house near Ostia, another species of filaria was found lying in the thoracic muscles. Bastianelli has also found similar nematodes developing between the thoracic muscles of these anopheles. The definitive host of these filariæ is as yet unknown, but from the fact that *Anopheles maculipennis* is usually found in houses and stables, it is very likely that it may be one or other of the domestic animals.

APPENDIX C.

Rhipicephalus annulatus (Say).[1]

See Plate XXV.

Ixodes annulatus, Say. Journ. Acad. Nat. Sci. Philad., ii, p. 75, 1821.

Ixodes bovis, Riley. Bureau of Animal Industry, 1868.

Boophilus bovis, Curtice. Journal of Comp. Medicine and Veterinary Archives, July, 1891, and January, 1892.

Rhipicephalus annulatus, Neumann. Mém. Soc. Zool. France, x, pp. 407—414, 1897.

Length of full-grown and distended female about half an inch (13 mm.); width, less than one third of an inch (7·8 mm.); colour, a dull leaden hue, turning to a deep brown or vivid red in alcohol, but changing to a relatively small extent in formalin. Subelliptical in form when viewed from the dorsal or ventral aspect, broader behind than in front, with rounded anterior and posterior ex-

[1] We are indebted to Mr. R. T. Pocock, F.Z.S., for the technical description of this species.

tremities, the lateral margin showing a shallow constriction on a level with the points of insertion of the legs of the fourth pair. Dorsal surface sparsely hairy in distended specimens, somewhat closely hairy in those that are fasting; marked with three impressed longitudinal lines or grooves: a median extending from the centre to the posterior border, and one on each side passing backwards from a point just behind the head-shield or *scutellum*, also almost to the hinder border, slightly diverging from the middle line from before backwards, and often interrupted in front of the middle of its length. Ventral surface impressed with three grooves corresponding to those on the dorsal side: the median or anal groove extending from the anus, and the lateral or genital grooves from the genital orifice to the posterior end, these grooves being subparallel in the anterior half of their length, and diverging somewhat abruptly on a level with the anal aperture.

Head-shield or *scutellum* small, not sharply differentiated from the rest of the dorsal integument; about one fourth longer than wide; wrinkled laterally, but otherwise not noticeably sculptured; its sides subparallel anteriorly, abruptly converging posteriorly with the posterior border elliptically rounded; eyes small, situated on the margins of the plate at its widest part. *Capitulum*, or shield that bears the mouth-parts and rostrum, short and broad, transversely hexagonal. *Palpi* (appendages protecting the rostrum laterally) very short, long, externally angular, and inferiorly crested; apical subconical; the second and third segments wider than segment short and subcylindrical. *Rostrum* or *hypostome* short and broad, about one fourth longer than wide, armed below typically with four rows of teeth. *Legs* slender, sparsely hairy; basal segment of first at most weakly bidentate posteriorly; apical segment armed beneath with a terminal spike, preceded, except on the legs of the first pair, by a smaller spike. ♂ much smaller than ♀, only about 2 or 3 mm. long. The dorsal scute grooved as in the ♀, covering the entire body, its anterior end pro-

longed in front on each side into two horns, of which the inner is the smaller, and embraces the base of the capitulum; furnished posteriorly with eleven festoons, and in the variety named *micropla* with a median caudal prolongation. Ventral surface provided on each side of the anus with a pair of long, horny, subequal, adanal plates, which extend as far forwards as the basal segment of the fourth leg. *Legs* robust, with basal segment large; that of the first leg shortly bidentate behind, produced into a forwardly directed prominence in front.

This species is cosmopolitan in its distribution, occurring in all tropical and temperate climates to the south of about the 45th parallel of north latitude. It lives parasitically upon mammals of various kinds, and as a carrier of the parasite of cattle hæmoglobinuric fever has gained world-wide notoriety. Curtice thinks that it was introduced early in the sixteenth century into the Spanish settlements of America, and thence spread with the cattle to all such places as offered suitable surrounding conditions. Its original habitat was perhaps the Mediterranean basin. Curtice further expresses the probability that cattle hæmoglobinuric fever, which was also called Spanish cattle fever, may have been introduced at the same time from the old world with the cattle and their ticks.

Two other species of *Rhipicephalus*, of equally wide distribution in virtue of their infecting domesticated animals and following the wanderings of civilised man, may at first sight be confounded with *R. annulatus*. These are *R. sanguineus*, Latr., and *R. bursa*, Canestrini. Although closely related to one another, these two may be readily distinguished from *R. annulatus*. The palpi are relatively longer, and externally convex, instead of short and externally angular. The basal segment of the first leg is strongly and deeply bidentate in both sexes, and the male is provided with a single short adanal plate instead of the pair that are present in *R. annulatus*.

R. bursa may be distinguished from *R. sanguineus* by having the scutellum as broad as long, and coarsely punc-

tured, and by the posteriorly more widely expanded adanal plate, etc.

Yet a third species of not uncommon occurrence upon cattle and beasts of burden is *Hyalomma ægyptium*, which is distributed over the countries of the Mediterranean, Africa, India, etc. This is a larger species than either of the three species of *Rhipicephalus*, the distended ♀ reaching a length of 20 mm. or thereabouts. It also has the rostrum and palpi very much longer, and the eyes away from the margin of the scutellum. Furthermore, there are two short adanal plates on each side in the ♂ which only just surpass the anus in front, while above them on each side there is frequently a single horny prominence.

Rhipicephalus annulatus does not pass from one host to another, as was at one time believed, but completes its life upon the same host. The larvæ, when they emerge from their egg-shells, possess only six legs and, apparently, no sexual organs. They do not develop unless they be placed on a suitable host. When placed on cattle their growth begins at once, and in about a week they undergo a first ecdysis, from which they emerge with another pair of legs and a pair of large stigmata behind them. They are now *pupæ*, and go on developing until, in about another week, a second moult leads to the adult stage, with perfectly developed reproductive organs. Fertilisation then takes place, and the female begins to distend enormously with the growth of the eggs and the large amount of imbibed blood. After about three weeks of parasitic life the mature female drops off to lay her eggs amongst the herbage. The eggs number from one to two thousand, and are laid one by one, and each one is in turn coated with a glutinous protective substance, which is secreted by a pair of racemose glands situated just under and within the head-shield. Oviposition lasts a considerable time, and while the pile of eggs grows larger the body of the animal contracts, until nothing more is

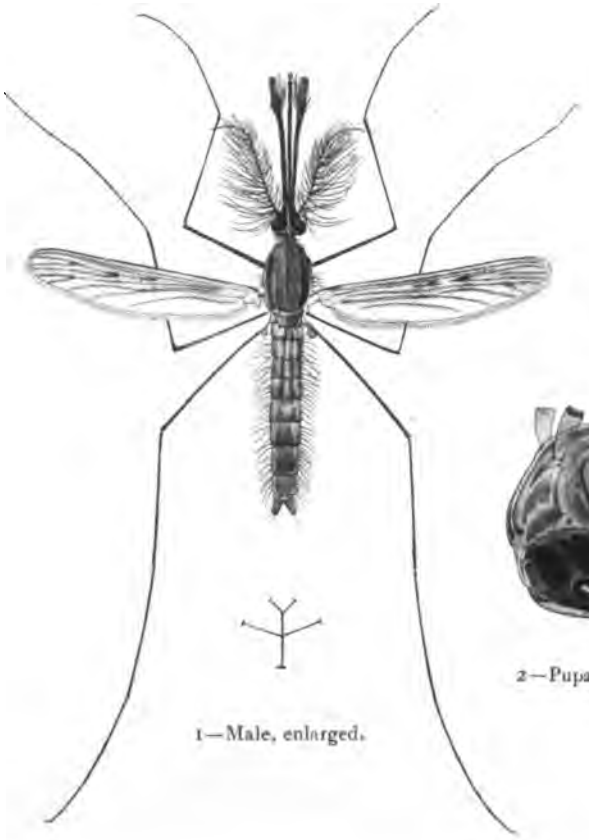
left than a yellowish, dried-up, shrivelled skin, whence all life has departed.

The eggs consist of a thin, shell-like covering, with a dark, opaque mass within. In the latter stages of incubation the form of the larval ticks becomes more and more apparent. The enormous quantity of blood imbibed by the female ticks serves for the development of their progeny; in fact, it becomes the vitellus with which the eggs are largely supplied, and residues of which may be seen within the abdomen of the newly-hatched larvæ. The most interesting feature in the experiments made by Smith and Kilborne is the demonstration that cattle hæmoglobinuric fever may be transmitted by ticks hatched in the laboratory, and that therefore the parasite must pass from the mother-tick to her progeny. This fact was at first generally discredited, but Koch repeated the experiment and confirmed it. However romantic it may seem, this fact is by no means unique; *Pebrine*, a protozoan disease of silkworms, is likewise transmitted, through the eggs, from the moth to the caterpillars.

As yet we know nothing of the exogenous cycle of *Piroplasma bigeminum*. The parasite has not been demonstrated in the salivary glands of ticks, but experiment has positively proved that it is inoculated by them. This may be explained by supposing that the parasites pass to the eggs with the vitellus which is derived from the infected blood imbibed by the fertilised female tick.

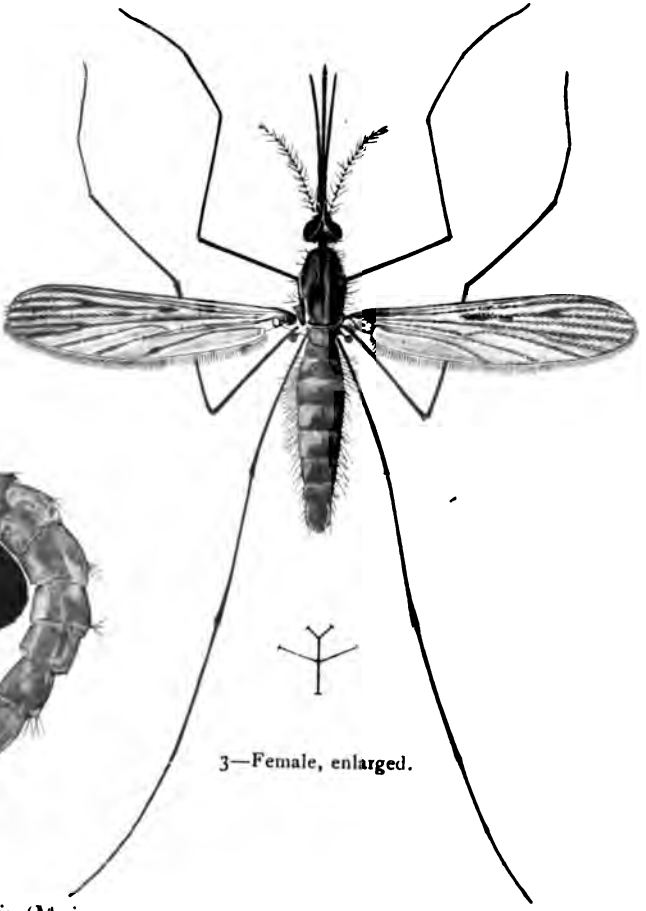
The *intra-ovum* inclusion of parasites is by no means uncommon; a trematode, *Distomum ovatum*, may be found occasionally in the white of the eggs of fowls, having been enveloped in the albumen during its excursions into the oviduct. Nematodes and other parasites have likewise been found enclosed in the eggs of fowls, ostriches, and other birds.

Probably the transmission of *Piroplasma bigeminum* occurs only through the fully-grown females at the time when, like the females of certain mosquitoes, they imbibe blood.



1—Male, enlarged.

2—Pupa, enlarged.



3—Female, enlarged.

Anopheles maculipennis (Meigen).

Drawn by A. Terzi.

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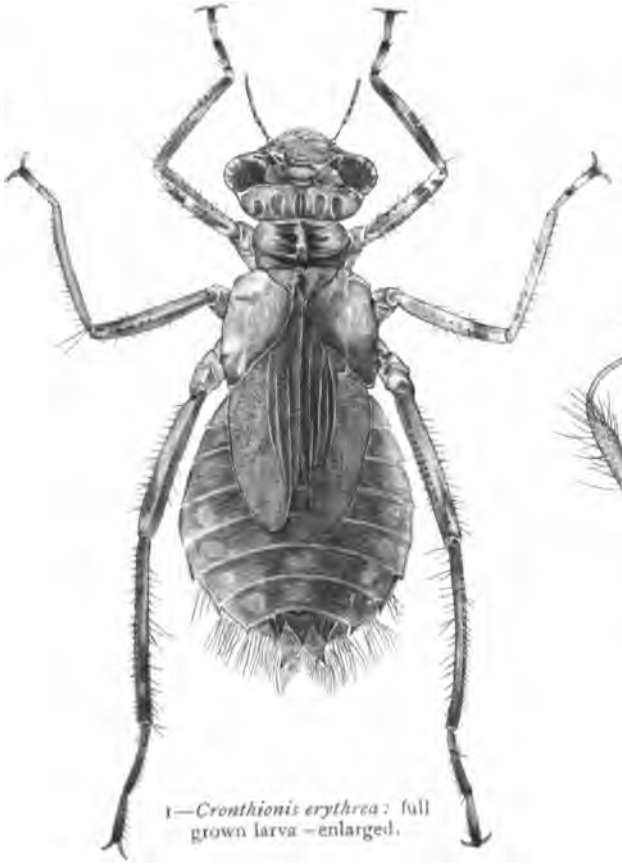
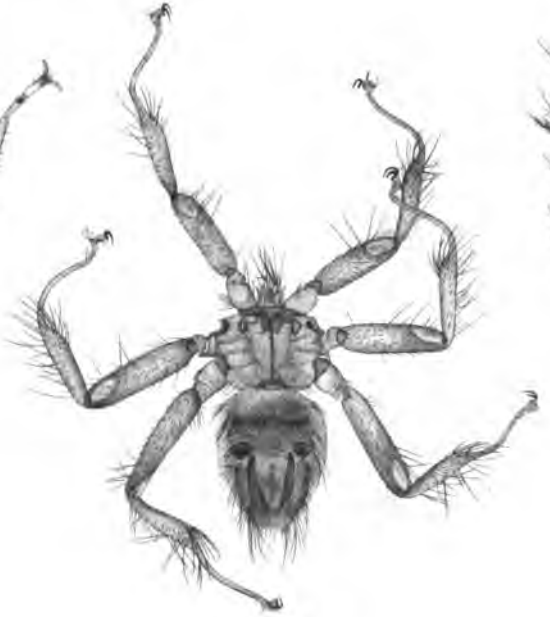


1—*Cronthionis erythrea*: full grown larva—enlarged.



2—*Nycteribia dufourii*: an ectoparasite of bats—enlarged.

3—*Anopheles maculipennis*: full grown *larva*—enlarged.

Drawn by A. Terzi.

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Driving a Herd of Buffaloes into Irrigation Canal for the purpose of weeding it.

(Drawn by A. Sartorio.) *Bale and Danielsson, Ltd.*

Buffaloes weeding Irrigation Canal—Pontine Marshes.

(Drawn by A. Sartorio.)

Bale and Danielsson, Ltd.

1—Full-grown female, ventral aspect—enlarged.

2—Full-grown female, dorsal aspect—enlarged.

3—Female depositing eggs.

4—*Larva*, ventral aspect—enlarged.

Rhipicephalus annulatus (Say).

Drawn by A. Terzi. *Bale and Danielsson, Ltd., Chromolith.*

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